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MASSIVE BLOOD REPLACEMENT

V. Failure to Observe Citrate Intoxication

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"CITRATE INTOXICATION" has been the subject of clinical and laboratory investigation since the advent of the modern blood bank with its ready supply of citrated whole blood. For a considerable period of time these investigations were mainly of academic interest. Adams in 1944 concluded that "a large margin of safety is present even in massive transfusions of citrated whole blood." However, the maximum rate of blood infusion in patients investigated by Adams at that time was 1,250 milliliters per hour. War injuries, cardiovascular surgery, and radical cancer operations often require massive quantities of blood and therefore have placed the problem of citrate intoxication in the realm of clinical reality. Before deciding whether other methods of preserving and storing blood are desirable, it is necessary to clarify the effects of citric acid upon the cardiovascular system and the clotting mechanism in the human being.

Acid citrate dextrose ACD solution, the anticoagulant used in bank blood in this country, is a source of considerable exogenous citrate acid. The most common ACD solution used is solution B of the National Institutes of Health. This solution contains 13.2 grams of trisodium citrate, 4.9 grams of citric acid, and 14.7 grams of dextrose diluted to 1,000 milliliters with distilled water. The citrated bank blood administered in the series reported in this article contained 120 milliliters of this solution in each bottle, or an equivalent of 1.43 grams of citric acid for each unit of blood.[1]

The concentration of citric acid in the nonred cell mass portion of bank blood (plasma plus ACD solution) cannot be calculated accurately from the total citric acid per unit of blood because of the varying

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[1]One unit of bank blood refers to approximately 480 milliliters of donor blood plus 120 milliliters of ACD solution.

TABLE I.—CITRIC ACID VALUES IN PATIENTS WITH ABNORMAL LIVER FUNCTION

Patient	*Citric acid in mgm. per cent*	*BSP ret., per cent*	*Ceph. floc., 48 hrs.*	*Thymol turbidity, units*
J.T.	2.0	11		
F.E.	0.1	3	3+	1.32
C.E.	0.1		3+	1.10
B.C.	0.3	10		
R.J.	0.7	24	3+	0.50
Y.F.	0.4	21		
M.S.	0.4			0.40
F.P.	0.2	16		
T.T.	0.2			0.35
R.G.	0.9			0.92
A.I.	0.7			0.40
B.S.	1.6	8		
B.J.	0.7	2		0.56
B.O.	2.2	5		0.33
W.O.	0.3	46		
G.R.	0.2	13		
S.M.	0.4			0.39
F.L.	0.2	9		
S.D.	0.1	6		0.26
A.B.	0.2		2+	1.33
D.A.	0.6	13		
M.B.	0.1	17		

hematocrit of donor blood, the nonconstant amount of blood added to the ACD solution, and the swelling of the red cells which occurs in the anticoagulant solution. Our determinations showed that the "plasma" citric acid of banked blood varied from 300 to 450 milligrams per cent and the washed red cells contained less than 1 milligram per cent of citric acid. In view of these variations, only the total equivalent amount of citric acid (1.43 gm.) in a given unit of blood can be utilized in determining the amount of exogenous citric acid administered with each unit of blood replacement.

Citric acid occurs endogenously and is a part of the Kreb's cycle (tricarboxylic acid cycle or cycle of terminal respiration). Its precursors are oxalactate and "active" acetate. A large quantity of citric acid is metabolized by muscle, the main site of carbohydrate metabolism, and it is readily metabolized through the stages of cisaconitic and isocitric acid in the presence of the enzyme aconitase. A daily oral intake of 40 grams of citric acid is oxidized completely in the body and is normally excreted in the urine at the rate of 0.20 to 1.0 gram per day. Whereas the excretion of citrate is decreased by parathormone, jaundice, severe liver disease, and thiamine deficiency, it is enhanced by alkalosis and the administration of bicarbonate, succinate, pyruvate and malate ions.

METHOD

In this report, the plasma citric acid[2] levels were determined by the Elliott modification of the method of Natelson, Pincus, and Lugovoy, as adapted for the Beckman DU spectrophotometer.

Plasma citric acid levels were determined in preoperative patients, in those with liver disease, in those to whom ACD solution was administered intravenously, and during and after blood transfusion in patients undergoing surgery, and during gestation.

1. The normal values were obtained from 120 patients prior to the administration of anesthesia, but after the patient had received the usual preoperative medication that would have been selected for the particular patient and operation.

2. Blood samples for citric acid determination were obtained in 22 patients who had abnormal liver function as measured by the bromsulphalein, cephalin flocculation, or thymol turbidity tests. These samples were obtained at the time blood was drawn for the liver function tests.

3. ACD solution (solution B of the National Institutes of Health) was administered to 3 patients anesthetized with thiopental nitrous oxide oxygen anesthesia and maintained at electroencephalographic level 2. Continuous electrocardiographic tracings were obtained during, and up to 40 minutes after, the administration of ACD solution. The ACD solution was administered intravenously at rates up to 40 milliliters per minute (8.6 mgm./kgm./min, citric acid) for 20 to 30 minutes, and venous samples were drawn from the opposite arm at regular intervals for citric acid, calcium, and potassium determinations. In 1 of these patients the following blood clotting studies were done: bleeding time, platelet count, prothrombin time, concentration of factor

[2]Citric acid refers to the anhydrous citric acid $C_6H_8O_7$, molecular weight, 192.1.

V (accelerator globulin) factor VII (proconvertin), prothrombin consumption, fibrinogen, euglobulin fibrinolytic activity, whole clot lysis, and antiplasmin. The methods used for these determinations are described in another article (23).

4. Plasma citric acid levels were determined on 77 patients during the transfusion of citrated bank blood. These patients received varying amounts of blood throughout the operative and recovery periods. When possible, venous samples were drawn before anesthesia, after the start of anesthesia, after the start of the operation, and at varying intervals throughout the operation, and during the recovery period. All samples were taken from an extremity other than that used for blood administration. During the 3 days following surgery, urine samples were collected from 3 patients who had received large quantities of citrated blood. These were analyzed for citric acid.

5. Blood samples for citric acid determinations were obtained from pregnant women. Six women were studied in the first, 54 in the second, and 55 in the third trimester of pregnancy.

RESULTS

One hundred and twenty-seven preoperative patients were studied, and the mean normal plasma citric acid levels were found to be 0.80 ± 0.8 (s.d.) milligrams per cent for men and 1.08 ± 0.9 (s.d.) milligrams per cent for women.

The results of the liver function tests and citric acid determinations in 22 patients are shown in Table I. The citric acid values were not appreciably elevated in the presence of abnormal liver function. The mean value for these patients was 0.57 ± 0.47 (s.d.) milligrams per cent.

There was a variation in the mean plasma citric acid level during the 3 trimesters of pregnancy. The mean values were: for the first trimester, 2.36 ± 2.5 (s.d.) milligrams per cent; for the second trimester, 2.04 ± 1.5 (s.d.) milligrams per cent; for the third trimester, $1.4 \pm .27$ (s.d.) milligrams per cent.

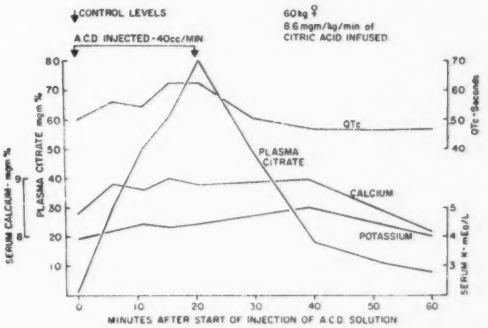

FIG. 1. QT_c interval and plasma citric acid, potassium, and total calcium during the infusion of ACD solution.

There is a significant difference between the mean plasma citric acid levels for the second and third trimesters ($t = 1.88$, for $P_{0.05}$ $t = 1.98$).

The 3 patients who received ACD solution received an equivalent of citric acid at rates of 6.25 to 8.6 milligrams per kilogram per minute. In all patients, there was a marked increase in the plasma citric acid level, the peak of which coincided with the termination of ACD administration. At the same time, there was an increase in the serum calcium and potassium level and a prolongation of the corrected QT interval as determined from the electrocardiogram. At no time was there any sign of tetany or hypotension. In a representative patient (Fig.1) who received citric acid at the rate of 8.6 milligrams per kilogram per minute, a rapidly elevated plasma citric acid level (79.6 mgm. per cent) was obtained at the time the ACD solution infusion was discontinued. This elevation was followed by a progressive fall in the plasma citric acid level until an almost normal value was obtained 40 minutes after the injection of the ACD solution (60 minutes after the start of experiment). Although no calcium was administered to this patient, the total serum calcium levels rose from a preoperative value of 8.4 to a high of 9 milligrams per cent shortly after the discontinuance of the injected ACD solution. The point of return of the patient's serum calcium level to the pre-experimental value

TABLE II.—CLASSIFICATION OF PATIENTS RECEIVING BLOOD

Units of blood	*No. of patients*
1 through 5	37
6 through 10	19
11 through 15	3
16 through 20	11
21 through 25	3
26 through 30	1
31 through 40	3
Total	77

coincided with the return of the plasma citric acid level to almost normal. Concomitantly, in this period, the serum potassium values also rose with the citric acid levels, although there was considerable lag in the development of the highest plasma potassium level, which eventually declined to the normal control value. As can be seen, the patient's corrected QT interval was prolonged and the highest recorded QT interval coincided with the highest citric acid level in this patient, but returned to a normal value before the plasma citric acid. The clotting determinations which were done at least every 10 minutes during this study showed no significant changes.

There was considerable variation in the plasma citric acid levels which were determined in patients receiving citrated bank blood during anesthesia, operation, and the recovery period. In patients to whom the blood was administered slowly, plasma citric acid levels were often not significantly elevated. The amount of blood given to the 77 patients studied who received transfusions is shown in Table II. Patients who received blood rapidly invariably had elevated plasma citric acid levels. The rate of blood infusion was the most important factor in determining the peak level of the plasma citric acid; the total amount of blood administered was less significant.

When the rate of infusion of citric acid was calculated in milligrams per kilogram per minute[3] (Fig. 2), it was found that a higher citric acid value was obtained at the higher rates of infusion. As a rule of thumb it was found that for rates of citric acid infusion up to 8.6 milligrams per kilogram per minute, the plasma citric acid was elevated 8 milligrams per cent for every 1 milligram per kilogram per minute of citric acid infusion. The exact relationship between rate of citric acid infusion and plasma citric acid is being more fully investigated and will be discussed in a subsequent article.

The turnover time of citric acid was found to be very short. Therefore, it is important to obtain blood samples during maximum infusion rates to appreciate the peak plasma citric acid level. The plasma citric acid levels of 3 illustrative cases are shown (Figs. 3, 4, and 5).

The highest plasma citric acid value recorded in our series was 173 milligrams per cent (Fig. 3). It was observed in a patient who received citric acid at a rate up to 4.8 milligrams per kilogram per minute (14 units of blood per hour Fig. 2). This patient was in profound shock and required rather rapid blood replacement. The blood sample obtained 2½ hours after the start of blood administration was obtained from the inferior vena cava. When the shock was corrected and rate of blood replacement slowed, the plasma citric acid level in this patient decreased. Clotting studies on this patient are reported in other articles (Patient W. W., 23, and Patient 3, 24).

The rapid variation of plasma citric acid levels due to alterations in the rate of administration of citrated blood or plasma can be seen from the record of Patient 22 (Fig. 4). The highest plasma citric acid value was obtained when blood was given most rapidly (3.8 mgm./kgm./min. of citric acid). As the rate of administration decreased the plasma citric acid level fell (6.4 hrs.), only to increase again when the infusion rate of citrated blood increased (7 hrs.).

Urine specimens were obtained on this patient for the 3 days following surgery and analyzed for citric acid. The results are shown in Table III along with the urine citric acid values obtained in Patients 37 and 59. In spite of the infusion of a large

[3]In calculating rates of citric acid infusion, the following equivalent total amounts of citric acid were used: antihemophiliac plasma (AHP) 250 cubic centimeters=1,200 milligrams. Serum albumin, 25 grams=50 milligrams.

amount of citric acid, the urine citric acid excretion was not markedly elevated.

Plasma citric acid levels obtained on a patient undergoing partial hepatectomy are shown in Figure 5. Again, the highest plasma citric acid value, 44 milligrams per cent, was obtained at the time of the most rapid infusion of citric acid, 3.7 milligrams per kilograms per minute. When the infusion rate of blood was slowed, the plasma citric acid promptly fell in spite of the fact that approximately one-half of the patient's liver had been removed by this time.

The slope of the decay curve of plasma citric acid is an indication of the rate of metabolism of citric acid. This slope is about the same as that observed in other patients who received similar quantities of blood at the same rate (24). The removal of a large portion of the liver did not seem to impair the ability to metabolize citric acid. However, as the wound was being closed, there was an oozing from the subcutaneous tissues and muscles. This oozing occurred despite the administration of 10 grams of calcium gluconate during the procedure. Blood clotting studies showed that this oozing was due to fibrinolysis and low fibrinogen. Clotting studies on this patient are reported in another article (Patient 4) (24).

Eighteen of the 77 patients studied during anesthesia and surgery developed clinical evidence of vascular oozing during the operative period. Clotting studies were obtained on these patients and are reported in detail elsewhere (23, 24). Two of these 18 patients in whom oozing was observed had received no blood, while 1 patient had received 9,000 cubic centimeters (15 units) in 2 hours. The plasma citric acid level in these patients varied from 1.3 milligrams per cent in a patient who received no blood to 173 milligrams per cent in the patient who received 30 units. The elevated plasma citric acid was secondary to the rapidity of bank blood infusion. There was no direct correlation between plasma citric acid level and oozing. All instances of oozing could be accounted for by changes in clotting factors. It should be emphasized that high plasma citric acid values, up to 44.7 milligrams per cent, were observed during surgery in patients who did not exhibit vascular oozing.

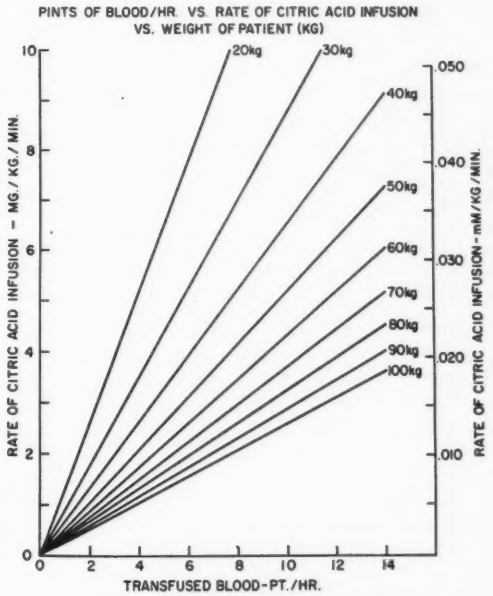

FIG. 2. Relationship between rate of bank blood transfusion and equivalent citric acid infusion.

CITRIC ACID VALUES OBSERVED

Citric acid is a normal constituent of blood plasma. Its concentration in plasma has been variously reported as 2 milligrams per cent and 1 to 2.5 milligrams per cent. We found the mean citric acid level for men to be 1.08 ± 0.9 milligrams per cent and for women, 0.80 ± 0.8 milligrams per cent. Some workers calculated citric acid as the monohydrate so that their values would be slightly higher. Values obtained by Thunberg's method have been reported to be slightly higher than those obtained by the pentabromoacetone method. Our values were from fasting preoperative patients and since fasting levels are lower than those postcibum, they are consistent with values which were previously reported by Mårtensson.

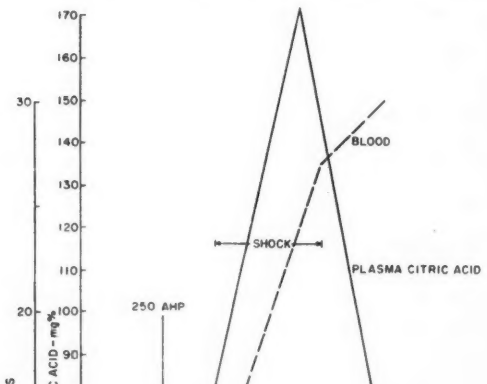

FIG. 3. Plasma citric acid levels observed in Patient 3.

Elevated plasma citric acid levels have been reported in patients with liver disease. In our study, we found the mean plasma citric acid in patients with liver disease to be 0.57 ± 0.47 milligrams per cent. Most of the patients in our series who had abnormal liver function tests had metastatic carcinoma to the liver. The patients with liver disease studied by Bunker and associates suffered predominantly from cirrhosis. Mårtensson showed that the liver was not necessary for metabolizing citric acid in the body. Therefore, it may be that metabolic disturbances associated with cirrhosis impair citric acid metabolism and might account for this discrepancy.

A significant difference between the citric acid values occurs during the second and third trimesters of pregnancy. This is not in agreement with earlier work that showed no change in the citric acid during pregnancy until just before the onset of labor. Shorr, Bernheim, and Taussky suggested that a relationship exists between progesterone levels and citric acid. From their work one would expect an increased plasma citric acid during gestation.

CARDIAC DISTURBANCES

The adverse effects of massive blood replacement have been reported as disturbances of cardiac function and failure of the blood clotting mechanisms (5, 10, 11).

Ventricular fibrillation and cardiac asystole have been the most serious cardiac complications (11). Premonitory electrocardiographic signs of impending cardiac disaster have been prolongation of the QT interval, widening of the QRS complex, elevation of the T wave, and bradycardia. These electrocardiographic changes have been reported to occur with hyperkalemia and hypocalcemia. Ventricular fibrillation will occur in nontransfused patients with depressed calcium levels, lowered *p*H, hypothermia, and elevated potassium levels. Citrated bank blood could create most of these disturbances. The plasma of stored bank blood will contain varying amounts of potassium depending upon the duration of storage, and potassium levels as high as 15 milligrams per cent may be approached. Bank blood is stored at 4 degrees C. and, when given in the operating room, is seldom above 6 to 10 degrees C. This can result in a lowering of body temperature. The *p*H of bank blood is usually 7.0 or below, and this can contribute to the development of acidosis. The oxygen dissociation curve of patients after transfusion is shifted to the left so that oxygen transport and carbon dioxide uptake may be impaired. Thus, during the rapid infusion of bank blood, multiple factors acting together may contribute to the development of cardiac abnormalities.

It would appear, from the data obtained in patients receiving the ACD solution at rates of 6.3 to 8.6 milligrams per kilogram per minute, that citric acid per se is not the

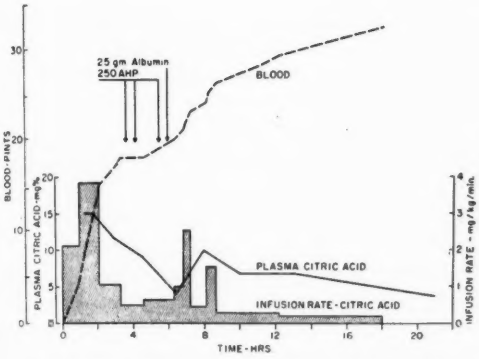

FIG. 4. Plasma citric acid levels observed in Patient 22.

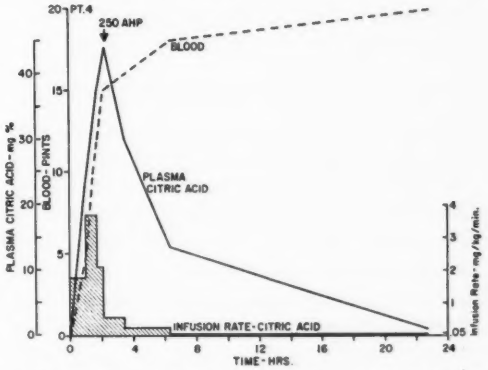

FIG. 5. Plasma citric acid levels observed in Patient 4.

etiologic factor in the development of cardiovascular abnormalities occurring during massive blood replacement, although it may contribute to their development. Certainly, the administration of ACD solution will result in a prolongation of the electrocardiographic QT interval. This prolongation of the QT interval following citrate was reported by Krautwald and Dorow. These investigators infused sodium citrate at different concentrations and at rates up to 8 grams in 4 minutes, in 25 conscious human volunteers. In addition to QT changes, they also observed tetany and clouding of consciousness. Total plasma calcium was not reduced during tetany; but the administration of calcium chloride would immediately counteract the symptoms produced by sodium citrate infusion. Chang and Freeman observed an increase in plasma total calcium when sodium citrate was infused into dogs. An increase in total calcium in humans receiving ethylene-diaminetetraacetic acid has also been reported. Our observation of an increased total calcium during ACD infusion in humans would confirm these results. Ames, Syllm, and Rapaport observed that there was a lack of correlation of the QT interval with plasma citric acid levels, since the QT interval returned to normal prior to the return of plasma citric to normal. Our observations confirm this work. When ACD solution was infused (Fig. 1), the QT_C interval increased as the plasma citric acid rose, but it returned to normal before the citric acid level did. It is possible that the citric acid bound ionized calcium so that additional calcium was mobilized from bony stores. Calcium exchange occurs very rapidly and follows an exponential function. Initially, it is possible that this could not compensate entirely for the reduction in ionized calcium produced by citric acid, or that it could not take place rapidly enough to keep the ionized calcium level within normal limits. Later (30 minutes, Fig. 1) the QT_C returned to normal while the plasma citric acid was still elevated, presumably because the total calcium had increased sufficiently to bring the ionized calcium within normal limits. We believe future investigations will show that the

TABLE III.—URINE CITRIC ACID EXCRETION IN MILLIGRAMS PER 6 HOURS

	Patient No.		
	22	*37*	*59*
Units of blood received	32	17	38
Hours, P.O. 0– 6	185	314	100
6–12	35	50	165
12–18	24	41	147
18–24	104	61	153
24–30	26	191	187
30–36	67	65	80
36–42	15	24	500
42–48	13	34	162
48–54	19	99	
54–60	15	114	
60–66	15	196	
66–72		194	
72–78		210	
78–84		152	
84–90		207	
90–96		138	

QT_C is correlated with the ionized calcium level during the infusion of citric acid.

IONIZED CALCIUM AND CITRIC ACID

Total calcium, protein, magnesium, and citric acid values have been measured and from these values attempts were made to calculate the ionized calcium by means of nomograms of McLean and Hastings. The results are not entirely consistent. This inconsistency may have arisen because the effect of *p*H on ionized calcium was disregarded. McLean and Hastings calculated from the factors of Van Slyke, Hastings, Hiller, and Sendroy a ratio for $\Delta\ Ca^{++}/\Delta\ p$H of -0.36. However, they were unable to demonstrate a change in Ca^{++} concentration of this magnitude for a change in *p*H. Recent work by Poulos (17) showed a mean value of -0.36 for Δ diffusible $Ca/\Delta\ p$H. Assuming the majority of diffusible calcium to be ionized, this means that a decrease in *p*H of .014 would cause an increase of Ca^{++} of .05 millimol per liter. Thus, studies in which ionized calcium was calculated and *p*H changes of 0.40 were ignored, are probably not valid.

The production of depressed ionized calcium levels with blood replacement has been the subject of much discussion. The greatest amount, 99 per cent, of the total calcium in the body is contained in bone. Less than 1 per cent is found in the blood and extracellular fluid.

Fifty to 70 per cent of the small portion of calcium in the blood is diffusible. Of the diffusible calcium in the plasma, most is ionized and is physiologically active, while a small part is unionized but diffusible. These equilibria were studied by McLean and Hastings who found equilibrium values for:

$$Ca^{++} = \frac{Ca^{++}Cit^{=}}{Cit^{=}} \times 10^{-3.22}$$

and

$$Ca^{++} = \frac{CaProt}{Prot^{=}} \times 10^{-3.22}$$

The level of total calcium in the plasma is normally closely regulated at 10 milligrams per cent. Important in maintaining this level are many factors such as intestinal absorption, renal excretion, and parathyroid activity. An excellent review of this problem was recently written by Copp. Evidence indicates that the calcium in the bone is primarily involved; in fact, the skeleton has an amazing ability to restore depressed plasma calcium to normal. Experiments have been carried out in which calcium was removed by lead phosphate, ethylene-diaminetetra-acetic acid, oxalate or citrate, and the body rapidly compensated and returned the plasma calcium to normal limits. Actually, the rate of calcium mobilization is directly proportionate to the lowering of serum calcium.

It is the ionized calcium which is physiologically active and in which we are interested. Saffran and Denstedt studied ionized calcium during administration of citrate. They found that the restoration of ionized calcium was very rapid even with high elevations of plasma citric acid. Reductions in ionized calcium were almost impossible to detect. This is not surprising since Falkenheim, Underwood, and Hodge showed by radioactive calcium tracer studies that calcium in bone is in an active state and can be readily mobilized. The rate of mobilization is limited by blood flow to the bone. Depressed ionized calcium is rapidly restored to normal, since the equilibrium between plasma ionized calcium and bone calcium is governed by the mass action law. Thus, if any factor tends to decrease the amount of ionized calcium present in the plasma there is a tendency for more calcium to become ionized. Available evidence indicates that the parathyroid hormone regulates the total calcium level, but that the skeletal calcium is primarily involved.

Citrate will bind ionized calcium. In effect, this disturbs the equilibrium between the ionized and nonionized calcium. Thus, from the mass action law it follows that some nonionized calcium in plasma will become ionized, and based on theoretic considerations, one would predict that the additional calcium will be mobilized from the

bone. This will cause an increase in the total plasma calcium. It is well known, and our results show, that total calcium increases when the plasma citric acid is elevated. It is evident, therefore, that even in the presence of an elevated plasma citric acid level and an increased total calcium, it is possible for the ionized calcium to be within normal limits.

Upon analysis of the 3 patients who received ACD solution and responded with an elevation of serum calcium, it becomes apparent that even though the exogenously administered citrate may deplete the ionized calcium in the patient's blood, the body mobilizes the readily available supply of calcium from the bone and this results in an increased total calcium. Thus, the elevated total calcium levels occurring with the administration of ACD solution probably reflect the action of a homeostatic mechanism of the body, which, in an effort to maintain ionized calcium within certain limits in the presence of an elevated citric acid, mobilizes calcium from the bone.

In the beginning of this study most of the patients received 1 gram of calcium gluconate (100 mgm. of calcium) for every 2 units of blood administered after the first 5 units. This was in accordance with the generally accepted belief that calcium is an effective antidote to citrate intoxication. Later, as it became apparent that citrate intoxication under normal circumstances did not exist, calcium administration was discontinued. The clinical course in the latter group of patients was not significantly different. Furthermore, patients who received ACD solution and no calcium did not exhibit citrate intoxication.

The plasma potassium concentration was observed to rise during the infusion of ACD solution. This rise was unexpected. Poulos (16) noted that plasma potassium and sodium concentrations fell during the infusion of calcium solutions. It is possible that the body attempts to maintain a plasma cationic balance and that an increase in plasma potassium during ACD infusion represents an attempt to keep cationic balance in the face of decreased ionized calcium.

CITRIC ACID AND OOZING

The development of vascular oozing during operative procedures has been found to be due to depressed platelets, and lowered fibrinogen, prothrombin, factor V, and factor VII. The presence of large amounts of citrated blood in the patient's vascular compartment could, possibly, result in blood that would not clot because of low ionized calcium, secondary to a larger amount of citrate. In this series citric acid was not found to have any relationship to the occurrence of vascular oozing. Both normal and elevated plasma citric acid levels occurred in the absence of vascular oozing. In the study previously reported (23), no correlation could be made between elevated plasma citric acid levels and disturbances in the clotting mechanism. In the controlled administration of ACD solution to a patient (Fig. 1), no significant changes were observed in the clotting mechanisms even though the plasma citric acid reached a peak of 79.6 milligrams per cent. Therefore, we believe that elevated plasma citric acid levels are not responsible for vascular oozing.

METABOLISM OF CITRIC ACID

The rate of metabolism of citric acid is very rapid. Citric acid is part of the normal metabolic pathway and many tissues are equipped with enzymes for metabolizing citric acid. It is metabolized notably by kidney cortex, liver, and muscle, the main sites of carbohydrate metabolism. A large amount, 70 per cent, is also stored in the bone.

When large amounts of citric acid are infused, it is possible that the normal enzyme systems for the metabolism of citric acid may become saturated. If this were to occur, the plasma citric acid value would increase out of proportion to that expected. Ordinarily, during the infusion of citrated blood, the plasma citric acid level is related to the extracellular fluid volume, rate of citric acid

infusion, and rate of citric acid loss. The citric acid loss from the plasma is due to several factors, the most important of which are: blood loss, metabolism, and loss of citric acid to tissues. Ordinarily, we expect an elevation in plasma citric acid on the order of 8 milligrams per cent for each 1 milligram per kilogram per minute of citric acid infusion. The peak value of 173 milligrams per cent attained in Patient 3 suggests the possibility of saturation. However, it must be pointed out that this sample was obtained from the vena cava and may not represent a mean plasma citric acid value, since mixing with peripheral blood in a patient in shock is not complete. However, the important clinical point is that a plasma citric acid value of 173 milligrams per cent was obtained from blood from the vena cava—blood that is entering the heart. This patient made an uneventful recovery. We have no idea what this patient's ionized calcium was, but his total calcium at the end of the procedure was 18 milligrams per cent. (Twenty grams of calcium gluconate was administered during the procedure.)

There is certainly a relationship between the rate of infusion of citric acid in milligrams per kilogram per minute and the plasma citric acid value observed. Except for Patient 3 in whom saturation may have occurred, we found that the rate of infusion and not the total amount of citric acid infused was the factor most important in determining the peak plasma citric acid value. In Patient 22, it can be noted that when the rate of infusion decreases, the plasma citric acid level decreases only to rise again, as the rate of infusion is increased. If one is to appreciate the relationship between plasma citric acid level and infusion rate, it is necessary to take frequent blood samples for citric acid analysis, especially during the peak infusion rates.

The liver has been shown to metabolize citric acid. However, it does not follow that it is the most important site of metabolism of citric acid. Patients 3 and 4, whose citric acid values are reported here, both had half the liver removed and in spite of this, metabolized citrate rapidly. In another paper (24), we compared the rate of metabolism of citric acid for Patient 4 with that of a patient undergoing a pelvic exenteration who had the same amount of blood administered in the same time interval. We could detect no appreciable difference in the turnover time or rate of citric acid metabolism. Mårtensson obtained the same results in animal experiments. Thus, in an acute experiment, the liver per se does not appear to be the most important site of citric acid metabolism. Bunker and associates reported that patients who suffered from cirrhosis metabolized citric acid poorly. It may be that factors other than loss of functioning liver tissue should be investigated to explain this observation.

Salant and Wise showed that the ability to recover from the toxic effects of citric acid was chiefly due to the rapid metabolism rather than to its excretion in the urine. Actually, urinary excretion of citric acid is increased only as long as the plasma citric acid level is elevated. Due to its rapid metabolism the citric acid remains elevated for only a short time. In our study of the urinary excretion of citric acid on 3 patients who received huge doses of citrate, we did not find the urine citric acid to be markedly elevated. Indeed, some of the patients excreted larger amounts of citric acid a day or 2 postoperatively than they did during the first 6 hours postoperatively. This may mean that factors other than plasma citric acid concentration are more important in determining the excretion of citric acid.

THE POSSIBILITY OF CITRIC ACID INTOXICATION

Citric acid may cause a toxic reaction because it has the ability to decrease the plasma ionized calcium and cause cardiac arrythmias or vascular oozing. Based on this premise, citric acid intoxication should be properly thought of as a deficiency of ionized calcium. In the present series we have not noted a complication that could be properly called citric acid intoxication.

What are the conditions under which hypoionized calcium can occur?

Under normal circumstances citric acid is metabolized rapidly so that toxic sequelae are not seen. If toxic sequelae are seen, they occur at the time citric acid is being administered most rapidly, since the metabolism of citrate occurs very quickly. Any factor that interferes with the body's metabolism of citric acid could contribute to citric acid accumulation. Hypothermia, whether induced or secondary to the infusion of large amounts of cold blood, will decrease the rate of citric acid metabolism. Perhaps longstanding liver disease with associated avitaminosis and malnutrition could contribute to faulty metabolism of citric acid. The possibility of saturation of enzyme systems has already been discussed. Patients who have hypoparathyroid disease, or osteoporosis, and cannot mobilize calcium may be more prone to citrate intoxication. Children, especially the newborn, may not have adequate calcium stores to draw upon, and therefore, may show signs of hypocalcemia. Shock with concomitant hypoxia could also conceivably contribute to a failure to metabolize citric acid, but a more important factor to consider in patients in shock is the failure of peripheral circulation. The circulation to bone is vital so that calcium can be readily mobilized. In states of shock it may be that the circulation to bone is diminished so that adequate calcium is not mobilized to keep the ionized calcium within normal limits during the infusion of citrated blood.

Of the factors that may contribute to citric acid intoxication, the latter is probably the most important.

We are essentially in agreement with Gruber and Halbeisen who studied the toxic effects of citric acid, and we believe that citrate intoxication during massive transfusion is unlikely.

SUMMARY

Plasma citric acid levels were measured by the pentabromacetone method in preoperative patients, in patients with liver disease, during gestation, during the infusion of ACD solution, and during and after blood transfusion. The highest value recorded in the series of 77 patients studied during transfusion, 173 milligrams per cent, was observed in a patient who received 30 pints of blood in 3.5 hours. This patient made an uneventful recovery. ACD solution was infused in 3 patients at rates up to an equivalent of 19 pints of blood per hour for 20 to 30 minutes. No change in clotting factors were noted, but the QT_c interval did become prolonged.

We believe that citric acid produces toxic effects by lowering the concentration of plasma ionized calcium. Citric acid is readily metabolized and most adults can mobilize calcium stores rapidly so that citrate intoxication under ordinary conditions does not exist. However, it is possible that children, hypothermic patients, and patients with impaired calcium metabolism or impaired circulation may be subject to citrate intoxication. Work by others has shown that intravenous calcium gluconate or calcium chloride given at the time the citrate is being administered most rapidly is an effective antidote. In this series, we saw no evidence of citric acid intoxication nor was there any difference between the clinical course of those patients who received calcium gluconate and those who did not receive calcium gluconate during rapid bank blood transfusion.

CONCLUSIONS

1. The normal mean plasma citric acid value for men is 0.80 $\pm$0.8 milligrams per cent, and for women, 1.08 $\pm$0.9 milligrams per cent.

2. The plasma citric acid value is not elevated in patients with metastatic liver disease.

3. The plasma citric acid is significantly lower in the third than in the second trimester of pregnancy.

4. When citrate is administered rapidly intravenously, there is an increase in the

QT_c interval, plasma potassium concentration, and total calcium.

5. The rate of citric acid metabolism is very rapid so that by 90 minutes after discontinuance of blood administration the plasma citric acid value is almost normal.

6. The plasma citric acid level during blood transfusion is related to the rate of blood administration.

7. The kidney is not the main pathway for elimination of citric acid.

8. Citric acid is readily metabolized by patients who have had a large portion of the liver removed.

9. There was no direct relationship between plasma citric acid values and the occurrence of vascular oozing.

10. Citric acid intoxication is unlikely in the normal adult during the administration of banked blood. Other physiologic changes occurring during transfusion are probably more important in causing vascular oozing and cardiac arrhythmias.

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FIBRINOLYSIS FOLLOWING THORACIC SURGERY

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OCCASIONALLY in thoracic surgery, bleeding problems occur which cannot be explained on the basis of a localized source of bleeding correctable by ligation. In most of these cases, profuse oozing from pin-point pleural areas or severe adhesions are encountered which generally cease spontaneously. Mathey and associates and de Geeter and Dumont have described 8 and 3 cases respectively of postoperative hemorrhage following thoracic surgery. Soulier and associates, in a study of 16 cases of thoracic surgery, demonstrated a shortening of the time of coagulation and complete lysis in 10 of the cases. Other authors have described single cases of severe hemorrhage following thoracic surgery.

In view of these findings, this study was initiated to investigate fibrinolysis of thoracic surgery patients in comparison with a number of general surgery patients. The results demonstrate a significant increase in lysis within 2 hours after thoracic surgery compared to a minimum increase after general surgery.

MATERIALS AND METHODS

Blood samples were drawn from 110 patients undergoing thoracic surgery. Of these, 79 were tuberculous and 31 were nontuberculous patients. The group consisted of 38 females and 72 males; 48 patients were between 20 and 29 years of age, 39 were between 30 and 39 years old, 5 were less than 19, and 18 were over 40. The types of operations were 11 decortications, 29 lobectomies, 60 segmental resections, 9 thoracotomies, and 1 pneumonectomy. The anesthetic used was sodium pentothal, intravenous, supplemented with ether during the operation.

As controls, bloods were taken from 40 general surgery patients, 19 males and 21 females. Seventeen were between 20 and 29 years old, 9 were between 30 and 39, 1 was less than 19, and 13 were over 40. The operations consisted of 11 partial or complete thyroidectomies, 7 hernioplasties, 5 cholecystectomies, 4 colostomies, 3 exploratory laporotomies, 2 excisions of parotid tumors, 2 mastectomies, 2 nephrectomies, 1 hysterectomy, 1 subtotal gastrectomy, 1 sympathectomy, and 1 ligation and stripping of veins. Thirty-five patients were anesthetized with sodium pentothal supplemented with ether, nitrous oxide, anectine, or combinations of these, 4 received only nitrous oxide and ether, and 2 received a spinal anesthesia of pontocaine.

Citrated venous blood samples (0.5 ml. of 10 per cent sodium citrate per 10 c.c. of blood) were drawn before surgery, immediately after the completion of surgery, and 1, 2, and 24 hours after surgery. In the thoracic operations, pulmonary arterial and venous blood samples were drawn during surgery. The plasma was obtained by centrifugation at 2,000 revolutions per minute for 10 minutes within 20 minutes after the blood was drawn. Two aliquots of each plasma were diluted 1:25 in 7.5×10^{-3} M calcium chloride solution and incubated for 45 minutes and 24 hours at 37 degrees C. Following each period of incubation, the fibrin was wound on a glass rod, washed with distilled water, pressed dry on filter paper, and digested in 0.5 milliliter of 20 per cent sodium hydroxide. When the fibrin was too fragile to be wound on a glass rod, it was obtained by centrifugation at 2,500

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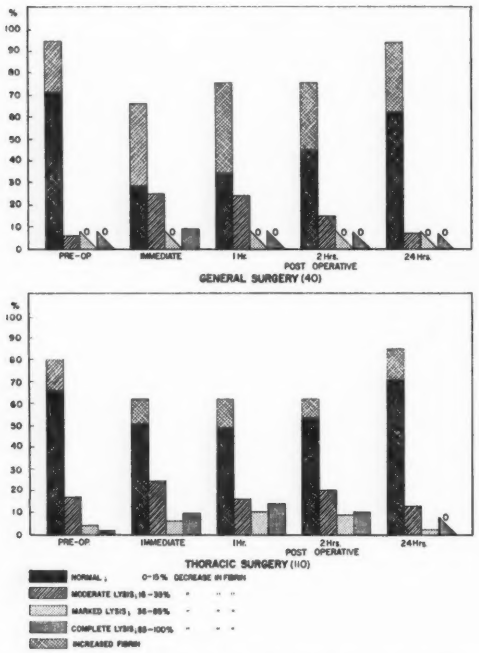

FIG. 1. Fibrinolysis following thoracic and general surgery.

revolutions per minute for 10 minutes and the supernatant decanted off. The amount of fibrin present was estimated by its tyrosine content according to the method outlined by Quick.

RESULTS

Fibrinolysis is expressed as per cent decrease in fibrin in 24 hours when compared with the amount of fibrin present after 45 minutes of incubation. The per cent decreases were arbitrarily grouped to indicate degree of fibrinolysis. A 0 to 15 per cent decrease in fibrin was considered normal, 16 to 35 per cent decrease was called moderate lysis, 36 to 85 per cent was marked lysis, and 86 to 100 per cent complete lysis.

The results from thoracic surgery and general surgery are shown in Figure 1. Each bar represents the per cent of patient plasmas demonstrating a certain degree of lysis at a given time before or after surgery. It can be seen that in general surgery only moderate lysis was demonstrated except immediately after surgery when complete lysis occurred in about 8 per cent of the plasmas. In the plasmas of thoracic surgery patients, 3 per cent showed marked lysis and 1 per cent complete lysis before surgery, while within 2 hours after surgery 6 to 10 per cent showed marked and 9 to 13 per cent complete lysis. Therefore, with this technique, a definite increase in fibrinolysis is observed following thoracic surgery when this is compared with the preoperative controls and with blood samples drawn at comparable times following general surgery.

Figure 2 shows a comparison of lysis in tuberculous and nontuberculous patients during and after thoracic surgery. The data suggest that surgical manipulation of a lung infected with tuberculosis causes no increase in lysis over a noninfected lung. Similar comparisons on the basis of age, sex, and time of year showed little difference in lysis. A slightly higher percentage of women showed complete lysis during surgery (Fig. 3).

The preoperative and postoperative fibrin levels are shown in Table I. Little change in the fibrin levels is seen within 2 hours after the operation, but when the preoperative and 24 hour postoperative levels are compared, a 31.0 per cent increase in fibrin is observed in the thoracic surgery patients and a 21.8 per cent increase

TABLE I.—FIBRIN LEVELS IN HUMANS FOLLOWING THORACIC AND GENERAL SURGERY

	Preoperative	*Postoperative*			
		Immediate	*1 hr.*	*2 hrs.*	*24 hrs.*
General surgery					
Mean (mgm.)	391	369	356	339	500
Standard deviation	±127	±98	±84	±74	±92
Thoracic surgery					
Mean (mgm.)	368	351	334	336	533
Standard deviation	±57	±69	±59	±75	±91

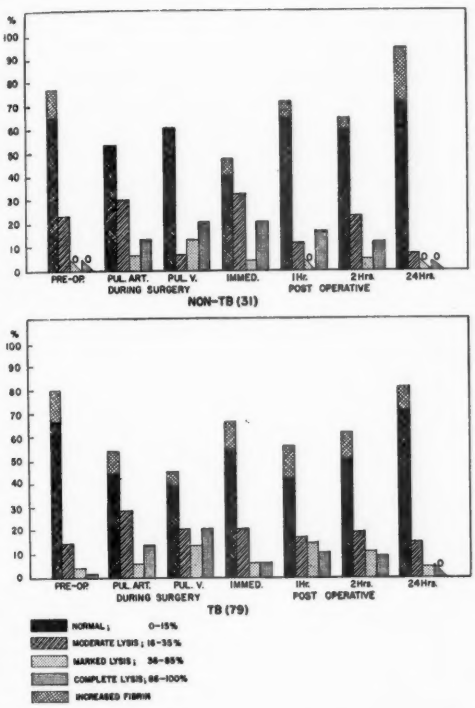

FIG. 2. Fibrinolysis in tuberculous and nontuberculous patients following thoracic surgery.

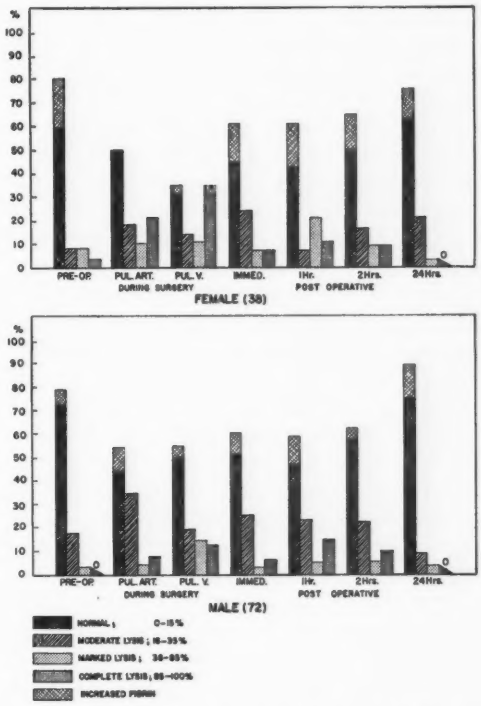

FIG. 3. Fibrinolysis in males and females following thoracic surgery.

in the general surgery patients. The fibrin levels of 9 thoracic surgery and 3 general surgery patients were determined daily for 10 days following surgery. In both types of surgery, a peak in the fibrin levels was observed at 3 days after operation (734 mgm. in thoracic surgery and 666 mgm. in general surgery patients) with a gradual decrease on the following days. The fibrin levels at 10 days after surgery are similar to those observed 24 hours postoperatively.

DISCUSSION

The majority of earlier investigations on the occurrence of fibrinolysis in general surgery have shown more postoperative lysis than the present study. Macfarlane (5) found complete postoperative lysis in 22 out of 29 surgical patients. Later, Macfarlane and Biggs (6) noted a similar preoperative increase in lysis which they attributed to anxiety. Variable degrees of lysis were found, both preoperatively and postoperatively, in surgical patients by Hodgson and Coon. These authors observed a similar increase in postoperative fibrin levels. Truelove found preoperative and postoperative fibrinolysis which could not be correlated with the severity of the operation. Three cases of severe hemorrhage associated with surgery were described by Blomback and associates in which increased spontaneous plasmin activities and decreased plasminogen contents were demonstrated.

An increase in fibrinolysis following various types of anesthesia has been demonstrated by von Kaulla. Since the same anesthesia was used in the majority of the thoracic and general surgery patients, the differences cannot be explained on this basis.

The higher per cent of thoracic surgery patients showing an increase in lysis, compared to preoperative samples and general surgery patients, can be correlated with the high concentration of tissue activator of plasminogen which has been demonstrated in the lung. Surgical manipulation of the lung could cause a release of the activator into the blood stream, causing an increased conversion of plasminogen to plasmin with a resulting increase in fibrinolysis. Further evidence favoring this hypothesis is the fact that during thoracic surgery the pulmonary venous blood shows a mean lysis of 134 milligrams of fibrin after 24 hours incubation, while the pulmonary arterial blood exhibits a mean lysis of 93 milligrams of fibrin, a difference of 30.6 per cent. This demonstrates that the plasmin content of the blood leaving the lung is higher than that entering.

Thirteen of the thoracic surgery patients showed hemorrhagic complications, i.e., oozing of blood during the operation or hemothorax following surgery. Of these 13, four showed moderate or marked fibrinolysis with this method and 8 (7.3 per cent) showed complete lysis during the operation or within 2 hours after the completion of surgery.

An attempt was made to utilize the synthetic amino acid ester methods in the estimation of fibrinolysis in surgical patients, but early results showed no correlation between the esterase and lytic activities and the use of the method was not continued.

SUMMARY

The fibrinolytic activity of plasmas from 110 thoracic surgery patients and 40 general surgery patients was investigated before, during, and after surgery. A slight increase in postoperative lysis was noted with the general surgery patients, while a significant increase was found in the thoracic surgery patients. In both thoracic and general surgery patients, an increase in fibrin was observed 24 hour after surgery.

Similar increases in fibrinolysis were seen in tuberculous and nontuberculous patients after thoracic surgery. No differences were noted on the basis of sex, age, or time of year, except for a higher incidence of complete lysis in the females during the period of surgery.

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A TRIAL OF ILEOSIGMOIDOSTOMY IN THE TREATMENT OF GASTROJEJUNOCOLIC FISTULA

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IT IS CERTAIN that as long as gastrojejunal anastomosis is used in the treatment of peptic ulcer there will be cases of anastomotic ulcer with some resulting fistulas. Undoubtedly the incidence of fistula has diminished with the greater use of partial gastrectomy in the treatment of peptic ulceration, and cases in future may be few, but, even if all patients operated on were subjected to partial gastrectomy, the complication of fistula would not be abolished, as it has been known to follow even fairly extensive gastric resection.

There seems to be little doubt that the logical treatment for gastrojejunocolic fistula is one stage obliteration of the fistula with partial gastrectomy, but by no means can all patients be considered fit for such an extensive proceeding. Certainly, in our series, not one was in good enough condition to permit of anything but minimal interference, at least in the first instance. The operation performed was a simple ileosigmoid anastomosis, lower than the ileocolostomy described by Lahey and Marshall. Gosset records symptomatic cure in 1 case following ileosigmoidostomy, and in this series the effects of the operation are assessed and further proceedings, in those cases in which it was necessary, are described.

In October 1947 the first ileosigmoidostomy in this series was carried out. Partial gastrectomy followed in a few months' time, but it was noted that there had been a remarkable recovery following the simple operation. Study of this case led us to the question "Is the second operation necessary or even desirable?" Lahey considered the ileocolostomy merely as a first stage procedure and followed it, when the patient's general condition had improved sufficiently, by partial gastrectomy and resection of the right colon to just beyond the fistula. We decided that, with future cases, ileosigmoidostomy alone would be performed, and that partial gastrectomy would be reserved for those patients who seemed to require further operative treatment. Since the first case, 5 further cases of gastrojejunocolic fistula have been treated, and in only 2 of these has it been considered necessary to carry out partial gastrectomy.

All the patients have been carefully followed up clinically. In those cases in which it was possible, the biochemical state has also been thoroughly investigated. As small intestinal hurry is the main factor in producing ill health in patients with gastrojejunocolic fistula, barium meal with follow through x-ray examination has been carried out on most of our patients after ileosigmoidostomy to ascertain the time taken for barium to reach the sigmoid. The results of our investigations, and the complications and difficulties encountered by us in this series, seem worthy of discussion.

None of these patients was initially treated by us, but we have not considered it necessary to consult the original records as it is clear they all suffered from duodenal or juxtapyloric ulceration in the first instance.

In this study we shall try to assess the value of ileosigmoidostomy alone as a means of treating gastrojejunocolic fistula.

CASE REPORTS

CASE 1. Mr. J. A., aged 37 years (in 1947), a ship's plater, in 1940 had had a posterior gastroenterostomy

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for a large chronic prepyloric ulcer with considerable stenosis. Six months after operation there were symptoms suggestive of stomal ulcer. In 1947 he was admitted to the hospital suffering from diarrhea, (5 or more large fawn colored stools daily) fecal eructation, vomiting of feculant material, considerable weight loss, loss of energy, and anorexia.

On examination this man was a moderately emaciated pale individual with marked edema of ankles and sacral region and with ascites. His blood pressure was 105/55, and his weight 8 stones 5 pounds. A barium enema showed a gastrojejunocolic fistula was made. A fractional test meal indicated a low hydrochloric acid and total acidity, and no stercobilin in any specimen. Fat balance test showed fat absorption of 80 per cent. Microscopic examination of feces showed that undigested meat fibers were present. Results of blood examination were: hemoglobin 12 grams per cent; red blood count 4,800,000 with normal films; serum protein 3.72 grams per cent; albumin 1.6 per cent; globulin 2.12 per cent.

At operation under general anesthesia, an end-to-side ileosigmoidostomy was performed. Three days after this proceeding further intervention was required for acute intestinal obstruction caused by herniation of a loop of ileum through the mesentery at the site of the ileosigmoidostomy. During convalescence the general condition was markedly improved. There was no vomiting, the foul eructations became very infrequent, his appetite improved, and the bowels moved 2 or 3 times per day, the stools being formed and of normal appearance but soft and bulky. The edema and ascites gradually disappeared.

Four months later, he was readmitted for partial gastrectomy; his condition was very satisfactory. His weight had increased by 8 pounds. The only significant biochemical findings were the serum protein of 5.03 grams per cent, albumin of 3.6 per cent, globulin of 1.43 per cent—a restoration of the normal ratio. Under general anesthesia, the gastrojejunocolic fistula was found to extend from about midtransverse colon to the stoma and was of narrow caliber. The fistula was dissected, the colon closed, and a retrocolic Polya-Hofmeister gastrectomy was performed without incident.

Four months after operation he was fit and well-nourished, having gained nearly 2 stones in weight. Follow-up continued till August 1952 when he was in excellent health, weighing 9 stones 10½ pounds. There was no dyspepsia and the bowels moved once per day with formed motions of normal appearance. The only abnormal radiologic finding was an excess of gas in the right colon.

The man's opinion was that the operation had been very successful and he was well satisfied, carrying out his work as a ship's plater without difficulty.

Case 2. Mr. J. C., aged 43 years (in 1948), a bartender (heavy work, long hours), in 1942 had had a posterior gastroenterostomy for duodenal ulcer with stenosis. In March 1948, diarrhea started, up to 8 stools per day, the stools being pale and offensive. He also had a copious foul vomit once daily. Gradually there developed swelling of face, arms, legs, and abdomen and numbness and tingling in the legs. His appetite remained good but there was considerable loss of weight. In May 1948 he was admitted to the hospital. He was a pale, sallow, undernourished, exhausted man with swelling of face, arms, and legs and with abdominal wall edema and ascites. Knee and ankle reflexes were absent. A barium enema demonstrated a gastrojejunocolic fistula of moderately large caliber. By a fractional test meal no fecal smell or fecal matter was noted, and there was a high fasting acidity, falling to low level after 1 hour. Fat balance test indicated a fat absorption of 63 per cent. At fecal examination for undigested food, none was found, but the stools were pale, fatty, and moist. Results of blood examination were: hemoglobin 11.2 grams per cent; red blood count 3,940,000 with normal films; serum protein 4.7 grams per cent; albumin 2.8 per cent; globulin 1.9 per cent, serum calcium 8.7 milligrams per cent. The prothrombin, bleeding, and clotting times were normal. Capillary fragility test (Hess) was positive.

On June 21, 1948, under general anesthesia, an end-to-side ileosigmoidostomy was performed. The improvement immediately was dramatic. The first postoperative stool was normal, and following this, while in the hospital, there were never more than 2 daily motions of normal appearance. The edema and paresthesia rapidly disappeared, and in 14 days there was no evidence of ascites. The knee and ankle reflexes did not return. On July 7, 1948 this patient had to be reoperated on for small bowel obstruction, a band being found across a loop of small intestine in the right iliac fossa but unconnected with the anastomosis.

The general condition then improved steadily and a further investigation was carried out 1 month later. A fractional test meal showed specimens of normal appearance and odor, except that little flecks of feces were present in the first 5 half-hourly specimens. Normal levels of acidity to 1½ hours, but at 2, 2½, and 3 hours the acidity was slightly above normal. Fat absorption was 77 per cent. Results of blood examination were: hemoglobin of 13.6 grams per cent; red blood count 4,260,000 with normal films; serum protein of 6.45 grams per cent; albumin of 4.4 grams per cent; globulin of 2.05 grams per cent; serum calcium normal.

This man was seen last in March 1952. His general condition had remained excellent. Since operation in 1948 "he had never felt better." He ate without restriction; there was no dyspepsia and no diarrhea. The motions were regular morning and evening, formed and firm. His weight had returned to his normal before the onset of his first ulcer trouble—9 stones 12 pounds. His own opinion of this operation

was that "it had been very well worth while." He was working in his old occupation as a barman, a laborious job with long hours.

He would not submit to any specialized investigation, and clinically was a normal healthy individual of robust physique and cheerful demeanor. A straight film of the abdomen showed no evidence of any undue collection of gas or feces in the right colon.

CASE 3. Mr. R. K., aged 70 years (in 1950), retired, in 1919 had had a gastroenterostomy for duodenal ulcer. On June 9, 1949, he was admitted to the hospital. There had been no digestive complaints following gastroenterostomy. However, 6 months before admission he began to have intermittent attacks of diarrhea, at least 3 motions per day. He began to feel tired, light-headed, and he lost weight. For 3 weeks, shortly after the onset of this illness, he had vomited yellow sour material once or twice per day. Since then there had been no vomiting. In addition, he suffered from precordial pain on excitement and breathlessness on exertion.

On examination this patient was a frail, anxious old man, having obviously lost weight, which, on admission, was 8 stones, the normal in health being about 11 stones. A barium enema showed a gastrojejunocolic fistula. Results of the blood examination were: hemoglobin 85 per cent; red blood count 5,000,000 with normal films; serum protein 4.6 grams per cent.

On June 30, 1949, under general anesthesia, a side-to-side anastomosis, terminal ileum to sigmoid, with exclusion, was performed. In March 1950 he had gained 2 stones in weight and was feeling well on an unrestricted diet. He had 2 loose motions daily.

On May 22, 1952 this man was readmitted for investigation and assessment. It was with great difficulty that he was persuaded to come into the hospital which indicated that the dyspepsia of which he now complained was mild. For a year following operation he had been completely free from indigestion and had then begun to have lower abdominal pain 4 to 5 hours after food, relieved by food, with recent occasional nausea and sour mouthfuls. Within the previous few weeks the attacks of discomfort had been more frequent. In spite of this, the appetite was good and he had gained further weight, which was now 10 stones 8 pounds. The bowels moved loosely, on an average of 2 to 4 times daily. There was still some precordial pain on excitement or exertion. Clinically he was still a somewhat frail looking old man but his state of nutrition was excellent and there were no significant clinical findings. A barium enema demonstrated the presence of a gastrojejunocolic fistula. A barium meal and follow through examination showed no evidence of stomal ulcer and did not demonstrate the fistula. Within 1 hour the stomach was empty and the meal was scattered in the small bowel. At 3 hours there was a trace of barium in the sigmoid. At 5 hours the sigmoid was well defined and some barium had passed backward into the descending colon. A straight film of the abdomen showed no evidence of stagnation of feces in the right colon. At fractional test meal there was no fecal smell or fecal matter, and a very slightly raised acid curve but fasting level normal and return to normal in 1¼ hours. Fat absorption was 90 per cent examination of feces for undigested food showed numerous undigested muscle fibers, also Charcot-Leyden crystals. Results of blood examination were: hemoglobin 90 per cent; 12.6 grams per cent; red blood count 4,700,000; white blood count 5,800, films normal; serum protein 6 grams per cent; albumin 4.2 per cent; globulin 1.8 per cent; serum calcium 11.7 milligrams per cent; prothrombin time normal; capillary fragility normal; bleeding time normal.

While in the hospital his weight increased to 11 stones and the symptoms of which he complained disappeared on light diet, which was not rigidly adhered to as the patient appreciated his visitors' gifts of indigestible delicacies. While under observation on a generous diet this man was symptom-free, and from impressions gained and knowledge of his home circumstances, it was concluded that dietary indiscretions played a large part in his discomfort. When last seen in April 1955 this patient was very well, clear skinned and well nourished and with no digestive disturbances. He had 2 to 4 loose motions per day.

His own view was that the operation had been extremely successful.

CASE 4. Mr. W. B., aged 43 years (in 1951), a coachbuilder (heavy work), in 1940 had had a gastroenterostomy for duodenal ulcer. In 1943, a stomal ulcer was diagnosed. An operation was carried out, apparently excision of the ulcer with reconstruction of the gastroenterostomy. In 1947 vagotomy was performed for stomal ulcer which had recurred in 1944. In 1950 he was treated medically for hematemesis.

In August 1950 he was admitted to the hospital under our care. For 7 months he had had intermittent attacks of diarrhea, an attack lasting 3 to 4 days and attacks being separated by intervals of 1 to 2 weeks, when bowel motions were fairly normal. During an attack there were 6 to 8 motions in 24 hours, the motions being loose, light colored, and foul-smelling. On admission his weight was 8 stones 6 pounds, there having been obvious weight loss. A barium enema showed a gastrojejunocolic fistula. A fractional test meal showed a high acid curve. All specimens had fecal odor and contained colonic material. The stools were bulky, pale, and fatty, containing undigested meat and other food. Results of blood examination were: hemoglobin 12 grams per cent; 86 per cent; red blood count 3,460,000; films normal; serum protein 5.5 grams per cent; albumin 3.6 per cent; globulin 1.9 per cent; serum calcium 9.5 milligrams per cent.

On September 4, 1950, an ileosigmoidostomy with exclusion was performed with side-to-side anasto-

mosis. The area surrounding the fistula was completely obscured by adhesions. When discharged from the hospital on September 20 the bowel motions were practically normal with only 2 per day.

In August 1951, he was admitted for assessment and investigation. His general condition was good. He had gained 1 stone in weight since the ileosigmoidostomy, his weight now being 9 stones 6 pounds and health normal. He had been well since his operation; he had no dyspepsia and had a good appetite. There had been, on an average, 2 motions per day, both formed and of normal size. He was back at his work as a coachbuilder and stated that he felt just as fit as he had been before all his ulcer trouble had started.

A barium enema demonstrated the continued presence of the gastrojejunocolic fistula. Following a barium meal a trace of barium was found to pass immediately to the colon, but otherwise passed normally through the gastroenterostomy to the jejunum. At 4 hours barium was present throughout the small bowel. At 7 hours the sigmoid had filled. There was also some filling of the descending colon, suggesting retrograde peristalsis. It was also noted that the cecum and ascending colon were filled with fecal matter, plus a little barium from the enema carried out 30 days previously. This remained quite static throughout this examination. After a fractional test meal no fecal matter or fecal smell was present in specimens. There was a moderately raised acid curve but the fasting level and level at 2½ hours were within normal limits. Fat absorption was 84 per cent. There was no evidence of an unduly high content of undigested matter in the feces. Blood examination showed a hemoglobin of 12.6 grams per cent; red blood count 5,770,000; films normal; serum protein of 6.75 grams per cent; serum calcium of 10.2 milligrams per cent; prothrombin time, capillary fragility, bleeding and clotting times were normal.

Since discharge from hospital, this patient has remained in very good health and maintained his weight, an occasional twinge of hunger pain occurring 4 hours after food being the only symptom. This pain does not worry him much as it is immediately relieved by food. Three to four pints of beer produce 3 loose motions per day, but usually there were only 1 or 2 formed or soft motions daily. Barium meal examination in June 1952 and June 1953 revealed no sign of stomal ulceration. Feces remain in ascending colon, shown on periodic roentgenograms, but the amount varies.

The patient himself is delighted with the result of the simple ileosigmoidostomy and feels so well he does not wish any further operative treatment.

Case 5. Mr. R. B., aged 51 years (in 1953), a machinist (not heavy work), had had a gastroenterostomy for duodenal ulcer in 1947. Nine months after operation symptoms very suggestive of stomal ulceration started. On September 7, 1949, he was admitted with watery diarrhea of 8 weeks' duration, the bowels moving at least 4 times daily. Undigested food had been seen in the stools, which were bulky and light in color. He complained also of breathlessness on exertion. On examination this patient was a pale man, showing obvious gross loss of weight. A barium enema demonstrated a gastrojejunocolic fistula. Blood examination showed a hemoglobin of 14.9 grams per cent (hemoconcentration); serum protein of 5.75 grams per cent; albumin of 4.60 per cent; globulin of 1.15 per cent; serum calcium of 12 milligrams per cent.

At operation under general anesthesia on October 27, 1949, a palpable mass was felt in the region of the gastroenterostomy stoma, which was not disturbed. An ileosigmoidostomy was performed with a side-to-side anastomosis, terminal ileum to sigmoid, with exclusion.

The general condition improved markedly and by the date of discharge, November 19, his weight was increasing and the bowels moving rather loosely, on an average of 3 times daily. Following discharge from hospital, the improvement in his general condition continued and was maintained. His weight returned to his normal, 10 stones 4 pounds. He had 2 to 4 soft and unformed bowel movements daily at regular intervals. He enjoyed his food, although occasionally he had very mild epigastric pain after food, relieved by food or alkali. So little considered by the patient were these symptoms that they were only mentioned on close questioning after his perforation occurred (*vide infra*).

He continued to enjoy very good health, stating that he "felt fit for anything," till November 1951, when he was admitted as an emergency with symptoms of a perforated peptic ulcer. Immediate laparotomy showed a perforation anteriorly of a stomal ulcer and the colic fistula was noted. The perforation could only be dealt with by separating the fistula, resecting the affected part of the colon, and reconstituting the gastroenterostomy. The condition of the patient did not permit gastrectomy and the convalescence was very stormy, but he eventually made a good recovery.

A postoperative barium meal and follow through showed a normally functioning gastroenterostomy. At 7 hours the sigmoid filled and there seemed to be movement from the sigmoid to the descending colon. A straight x-ray film of the abdomen showed no abnormal gaseous or fecal collection in the cecum or ascending colon. A fractional test meal showed a climbing acid curve well above normal. Following this operation the patient had 2 formed motions daily and enjoyed good health till March 1952 when he began to have dyspeptic symptoms of peptic ulcer type. By November 1952 the ulcer symptoms were more persistent and in spite of 2 previous negative barium meals, readmission for partial gastrectomy was decided upon.

At operation under general anesthesia on December 4, 1952, a large deep chronic jejunal ulcer was found, ¾ inch in diameter, of the efferent loop just distal to the stoma. There was marked pyloric stenosis but no active duodenal ulcer. A partial gastrectomy, four-fifths of stomach, with antecolic anastomosis, was performed with end-to-end junction of the jejunum following resection of the ulcerated area. One month after discharge from the hospital there was an attack of severe abdominal pain, relieved by an enema with a large fecal evacuation. An x-ray film following the enema showed a large collection of gas in the right colon. Some anxiety, therefore, was felt about stagnation in the right colon. It was thought that the colic was due to this, and it was decided to undo the ileosigmoidostomy.

At operation under general anesthesia on February 6, 1953, the cecum and ascending colon were not distended. The blind loop of ileum beyond the ileosigmoidostomy was grossly dilated and the stoma had stretched to between 3 and 4 inches. The ileosigmoid anastomosis was undone and the sigmoid closed. The dilated ileum was resected and end-to-side anastomosis of ileum to cecum performed. It was noted that the cecum contained feces and succinylsulfathiazole which had been given preoperatively.

Postoperatively there was a fair amount of distention which caused some trouble, but the bowels moved on the eighth postoperative day and the distention lessened. On the following day there was very severe abdominal pain and the patient became extremely shocked. The abdomen was grossly distended and the diagnosis was that of fecal perforation due to breakdown of anastomosis. The deterioration was so sudden and complete that a further exploration could not be undertaken, and although the patient survived for 4 days he was never in condition to permit laparotomy.

At autopsy the abdomen showed general peritonitis with small pockets of pus throughout the peritoneal cavity. There was gross congestion in the ileocecal region and there had been perforation at the site of the ileocecal anastomosis.

It seems that the postoperative distention had impaired the blood supply of the anastomosis and this had given rise to perforation and peritonitis.

CASE 6. Mr. H. B., aged 27 years (in Feb. 1953), a taxi hirer (not heavy work but long hours, had had a perforated duodenal ulcer repair in 1946, a repair of a perforated duodenal ulcer plus gastroenterostomy in 1950, and in January 1952 he was admitted under our care with a stomal ulcer. Marked response to an insulin test meal produced hypoglycemia.

At operation under general anaesthesia on January 30, 1952, just beyond a posterior gastroenterostomy stoma, the jejunum was seen to be red and angry looking and appeared to be the seat of an ulcer. Transabdominal vagotomy was performed. At a postoperative insulin test meal, no response to injection of insulin was noted. Following this operation he remained well and was back at work until June 1952.

On July 3, 1952, he was readmitted to the hospital, having had marked diarrhea for 3 weeks, the motions being frothy and fatty looking with an offensive smell (5 to 7 motions per day), and there had been vomiting for 10 days (3 to 5 times per day). No pain but occasional giddiness was present. Examination revealed a pale ill man, showing marked loss of weight. His weight was 8 stones 6 pounds (normal about 10½ stones). Barium enema and barium meal x-ray examinations established the diagnosis of gastrojejunocolic fistula. Results of other investigations were: to a fractional test meal, a high climbing acid curve; to an insulin test meal, no response to injection of insulin; to fat balance test, fat absorption of 50 per cent; to examination of feces for undigested food, no undigested food particles seen; of blood examination, hemoglobin 95 per cent 13 grams per cent, red blood count 4,190,000, white blood count 4,800, blood film normal, serum protein 6 grams per cent, serum calcium 10 milligrams per cent, prothrombin time 20.5 seconds, control 16.0 seconds, capillary fragility normal, bleeding time 2 minutes, clotting time 5 minutes.

At operation under general anesthesia, the transverse colon was found adherent to the stoma. A side-to-side ileosigmoidostomy was performed with exclusion. Until January 1953 he was very well. He had no complaints at all, his bowels moved twice per day at most, the motions being soft and somewhat lighter in color than normal, and his weight went up to 10 stones 7 pounds. On February 3, 1953, he was readmitted to the hospital with acute symptoms of 3 weeks' duration, typical of recurrence of peptic ulceration. The patient was ill and his weight had fallen to 9 stones 13 pounds. A barium meal and follow through showed no abnormality in the stomach, the stoma functioning well and being of normal appearance; no ulcer was seen nor filling of the duodenum. The follow through up to 6 hours showed no intestinal hurry. There was no barium in the sigmoid at 6 hours, but the distal ileum was then filled. From 4 hours onward the hepatic flexure contained barium, presumably reaching it through the fistula. Response to a fractional test meal was a high climbing acid curve. Blood examination showed serum proteins of 7.75 grams per cent. In spite of negative barium meal, it was considered that there had been recurrence of stomal ulceration, and in view of the rapid onset of deterioration and previous experience, it was decided to perform partial gastrectomy.

At operation under general anesthesia on February 12, 1953, very many adhesions were present in the upper abdomen, and there was marked thickening

present around the stoma. A gastrojejunocolic fistula was found but no stomal or jejunal ulcer was demonstrated. A partial gastrectomy, with separation of the fistula, was performed, the anastomosis being antecolic. The ileosigmiodostomy was inspected and some dilatation of the blind end of the ileum was noted. Since this operation the patient has been very well. His weight went up to 10 stones 5 pounds. He has one formed bowel motion daily. No time has been lost from his work and he takes a normal diet. Straight x-ray film of the abdomen in 1953 showed a fairly large amount of feces in the cecum and ascending colon.

DISCUSSION

The complication of gastrojejunocolic fistula formation results in diarrhea and vomiting, and, of these two symptoms, diarrhea predominates. The patient may pass many motions in the course of 24 hours, and these motions are loose, bulky, and fatty in character. It is remarkable that remissions of symptoms may occur, as shown in 2 of our cases (Cases 3 and 4) and this is difficult if not impossible to explain, as it is quite obvious that the fistula once formed remains patent. Typically, ulcer pain disappears with the formation of the fistula, and the stomal ulcer heals, possibly because of the neutralizing effect of the colonic contents on the gastric juices. Lowdon suggests that the tendency for the ulcer to heal after the formation of a fistula may be explained by the gastritis, which commonly occurs in these patients, tending to reduce the gastric secretions. As a result of the diarrhea and vomiting, the patient loses weight, and in severe cases becomes emaciated and critically ill. Marked biochemical disturbance may occur with resulting edema and ascites. Peripheral neuritis may be a feature in bad cases.

The diarrhea and vomiting are caused by the passage of colonic contents into the jejunum via the fistula. The diarrhea is not caused by stomach contents passing directly into the large bowel. It can be shown by barium meal that very little of the stomach contents passes to the colon direct, in fact it is often impossible to demonstrate a gastrojejunocolic fistula by means of barium meal. However, by means of barium enema, a gastrojejunocolic fistula is usually easily demonstrable. The colonic contents, having reached the stomach and jejunum, pass down the small bowel and give rise to irritation and small intestinal hurry. Bolton and Trotter were the first to realize that the diarrhea was the result of the colonic contents irritating the jejunum. Lowdon records the presence of gastritis and jejunitis in these patients, attributable to irritation by colonic contents. As a result of the jejunitis, food taken by mouth is rushed through the small bowel, allowing very little time for digestion and absorption. This produces the fatty diarrhea, progressive loss of weight, and emaciation, so typical of the established case of gastrojejunocolic fistula.

The ideal treatment for gastrojejunocolic fistula is closure of the fistula and partial gastrectomy, and, in those patients who are fit for this major procedure, this is the treatment of choice. Most patients are not fit for such a lengthy operation, and in these the object of the first operation must be to improve the patient's general condition so as to make him fit for partial gastrectomy later on if required. Various methods have been used with this object in view. Wilkie (1934) described division of the transverse colon on either side of the fistula with closure of the ends of the small piece of large bowel left attached to the stomach and jejunum and end-to-end anastomosis of the transverse colon. Pfeiffer and Kent recommended proximal defunctioning colostomy in the ascending colon. Lowdon described transverse defunctioning colostomy just proximal to the fistula. In Lahey's operation, the ileum is divided at the cecum, the distal end closed, and the proximal end anastomosed to the descending colon with an antiperistaltic side-to-side anastomosis.

In our series, an ileosigmoid anastomosis was performed with an isoperistaltic side-to-side anastomosis, except in the first 2 cases in which an end-to-side anastomosis was used. The end-to-side anastomosis was given up because of the complications which were encountered.

The advantages claimed for ileosigmoidostomy is that it is a simple procedure, disturbing the patient very little, and it can restore health sufficiently to allow much more extensive proceedings to be carried out. Indeed, in some cases it restores the general health to such an extent as to obviate the necessity for further operative treatment. Of course, proximal colostomy is also a simple proceeding, but no patient would choose to have a colostomy, even though temporary, if he were given the choice of an equally safe operation which did not necessitate the construction of an abdominal anus. In addition, no surgeon would consider a permanent colostomy as the ideal treatment for gastrojejunocolic fistula. In those cases in which partial gastrectomy is ruled out because of poor general health, as in our Case 3, if a colostomy has been performed the patients are condemned to having a colostomy for the rest of their lives. On the other hand, a permanent ileosigmoidostomy would be acceptable to patient and surgeon alike in those cases in which partial gastrectomy is considered unnecessary or inadvisable. Even in a healthy young adult, partial gastrectomy carries with it a small mortality, and, because of this, it seems unwarrantable interference to operate further if excellent results can be obtained with ileosigmoidostomy alone. If a colostomy has been performed, further operative treatment is essential to avoid leaving a young fit patient with a permanent colostomy. Lowdon argues in favor of proximal transverse colostomy that the Lahey shunt is a more formidable procedure and that the second stage involves sacrifice of half of the colon. We believe that ileocolostomy is a simple operation involving little more risk to the patient than proximal colostomy and that, at the second stage, if a second operation is required, the colon may be left in situ.

If a patient is left with a permanent ileosigmoidostomy it is essential that he be kept under observation for some considerable time and, when finally discharged, he must be warned that the onset of ulcer symptoms must be the signal to him to seek medical advice. Our experience (Case 5) and the experience of others have shown that an ulcer may develop in the presence of a fistula, which, of course, is still present in these patients, and that lack of treatment may lead to dangerous complications. Lowdon noted the presence of peptic ulcers adjacent to the fistula in 4 of his series, and 1 of his series had a perforation of a second ulcer. Also Lion and Moveau, Barling, and Hurst and Stewart reported the occurrence of free perforation of a second peptic ulcer in the presence of a fistula.

Case 2 is the perfect result from ileosigmoidostomy alone. No further improvement can be expected. He is asymptomatic and in excellent general health. There could be no justification for performing partial gastrectomy on this man. In this case the second operation is neither necessary nor desirable. It is presumed that he still has a fistula although investigation to prove this has not been possible. The pathologic characteristics of gastrojejunocolic fistula would make spontaneous closure practically an impossibility as the fistula becomes lined with epithelium soon after its formation.

In Case 3 the second operation is perhaps desirable but not necessary or advisable. His general condition precludes a major procedure, such as partial gastrectomy and closure of the fistula. His fistula troubles him little, provided he avoids dietary indiscretion. This is an example of the other type of case in which permanent ileosigmoidostomy may be the operation of choice—a patient whose general health will not permit partial gastrectomy and in whom the result of ileosigmoidostomy is satisfactory although by no means perfect.

Case 4 is not a perfect result, neither is it a failure. This patient has an ileosigmoidostomy and nothing further has been done. He has symptoms suggestive of recurrence of stomal or jejunal ulceration although roentgenograms have failed to demonstrate an ulcer. However, it is notoriously difficult to demonstrate an anastomotic or jejunal

ulcer radiologically and it seems likely that he has further ulceration. Ideally, a partial gastrectomy and closure of the fistula should be carried out. On the other hand, he is well pleased with his present state, he feels well, he is doing a heavy job without difficulty, he is not restricting his diet in any way and he does not want anything further done. In fact, he is delighted with the result of the operation. What symptoms he has are very mild and, in addition, it is known that partial gastrectomy might well be hazardous because of dense adhesions surrounding the fistula. On balance, it was decided that the wisest course was to leave him alone but to keep him under supervision. Eventually this particular patient may well come to gastrectomy.

Apart from Case 1, 2 of our patients, Cases 5 and 6, had a partial gastrectomy with closure of the fistula. In both, symptoms of recurrent ulceration occurred following ileosigmoidostomy and these symptoms were causing the patients considerable disability, a quite different picture from that presented in Case 4. There was no doubt that these 2 patients required partial gastrectomy. In neither of them, nor in Case 1, was the right colon sacrificed as in Lahey's operation. The patients of Cases 1 and 6 are in excellent health following partial gastrectomy, but it is worthy of note that the patient in Case 2, with an ileosigmoidostomy only, is in equally good health.

In Cases 5 and 6, in whom partial gastrectomy and closure of the fistula were delayed until recurrent ulcer symptoms demanded further operative intervention, it will be noted that the fractional test meal after ileosigmoidostomy in both cases revealed a high climbing acid curve. This is in contrast to the 3 patients who have not had a partial gastrectomy, in all of whom the acid curve in the fractional test meal, following ileosigmoidostomy, is practically normal. These findings are important and significant. We are of the opinion that, if a patient, after ileosigmoidostomy, develops ulcer symptoms, a fractional test meal should be performed, and if this reveals a high climbing acid curve, the patient should be submitted to partial gastrectomy and closure of the fistula. If, on the other hand, the ulcer symptoms are mild and the fractional test meal within or near normal limits then it is permissible, at least, to consider no further operative treatment, as we have done with Case 4.

The immediate result following ileosigmoidostomy is dramatic. Frequently there are no more loose bowel motions while the patient is in the hospital and he settles down to 1 or 2 formed motions daily. Once he starts getting up and following discharge from hospital, the number of bowel motions per day may increase slightly. They are usually formed, but in 1 case (Case 5) they were soft and unformed and in another (Case 3) they were loose. In this series, the number of motions per day has been from 1 to 4. It is interesting that, in Case 3, the worst from the point of view of frequency and consistency of motions, the state of nutrition is excellent. None of the patients find the slightly increased frequency of bowel movement an inconvenience. All signs and symptoms of gastrojejunocolic fistula clear up, the weight steadily increases, and there is a feeling of general well being. All of the patients with ileosigmoidostomy only have reached their normal weight and are maintaining this weight. Clinically the state of nutrition following ileosigmoidostomy is excellent.

Some of the investigations carried out before ileosigmoidostomy are of particular interest:

1. Fat balance test.—The percentage of fat absorption was low in the 3 cases in which this test was done.

2. Fecal fat estimations.—The results have not been recorded in the case records of our patients as it was not found possible, in the stress of more necessary work, to perform repeated investigations, and we recognize that this is necessary to obtain conclusive and valuable results. However, the results did show an abnormally high fat

content in the stools with a high proportion of unsplit fat.

3. Blood examination.—Mild anemia was present in all but Cases 5 and 6. The high hemoglobin per cent in Case 5 is presumed to be due to hemoconcentration as he was anemic looking. Anemia is the usual finding in cases of gastrojejunocolic fistula, but its presence may be missed on hemoglobin estimation owing to hemoconcentration as a result of dehydration.

4. Serum proteins.—These were low or low normal in all cases, as is usual, with reversal of albumin globulin ratio in Case 1. Apparently, this reversal of albumin globulin ratio must be uncommon, as Lowdon found no instance of it in his large series.

5. Serum calcium.—Serum calcium may be depleted in severe cases, so it is not surprising to find it low (8.7 mgm. per cent) in Case 2. In none of our cases were there carpopedal spasms, which may occur in the presence of gastrojejunocolic fistula, but in Case 2 there was paresthesia which could be attributed to the low serum calcium or might have been the result of vitamin B deficiency.

6. Prothrombin time.—Prolongation of this time has been noted by Atwater, Butt, and Priestley and occurs in 1 of our patients (Case 6).

7. Capillary fragility.—This was present in Case 2 and could be attributed to deficient absorption of vitamin C.

A patient suffering from gastrojejunocolic fistula often urgently requires operative intervention and, as a result, interesting investigations, apart from those required to establish the diagnosis, have, in many of the cases, not been performed, as it was not in the interest of the patient to delay operation further. This study is of little consequence as far as our investigations are concerned as it was not our object to compare preoperative and postoperative states so much, as to compare patients with ileosigmoidostomies with normal individuals.

Apart from the question of operative technique and the possibility of late complications after ileosigmoidostomy, our object was to discover whether patients suffered from any deficiency state following the operation. It must be remembered that the gastrojejunocolic fistula is still present, and one depends on short circuiting the fistula to produce results. It has been stated previously that small intestinal hurry is the cause of deficient digestion and absorption of food ingested, and hence is the cause of the severe deficiency state which is liable to develop before treatment is instituted. Ileosigmoidostomy corrects this intestinal hurry, but it cannot be said that it completely abolishes it except, perhaps, in 1 of our patients (Case 2) whose motions were reduced to 2 per day, formed and firm, normal in appearance, and occurring regularly morning and evening. It might be claimed that the patient in Case 4 is practically normal, but the fact that 3 to 4 pints of beer produces 3 loose motions per day probably indicates that there is still some intestinal hurry present. The effect of closure of the fistula illustrates that there must very often still be some intestinal hurry following ileosigmoidostomy. After ileosigmoidostomy, Case 6 was very satisfactory as far as frequency and consistency of bowel motions were concerned—2 soft motions per day—but after partial gastrectomy this patient had only 1 formed motion per day. In Case 5, following ileosigmoidostomy, the patient passed 2 to 4 soft and unformed motions per day, but following his perforation when the fistula was closed and the gastroenterostomy redone, his motions were reduced to 2 formed motions per day. In Case 1, following ileosigmoidostomy, the patient passed 2 to 3 formed motions per day, but after partial gastrectomy passed only 1 formed motion daily.

Thus the correct conclusion, from this study of the number and consistency of stools, would appear to be that ileosigmoidostomy reduces intestinal hurry considerably but does not usually, if ever, abolish it.

As a slight degree of intestinal hurry is present clinically in all but 1 of this series,

we set out to discover if there was deficient intestinal absorption and any evidence of a deficiency state which could not be elucidated by clinical examination.

It was decided that the most accurate measure of intestinal absorption could be obtained by the fat balance test, as recommended by Frazer (4), which had been carried out in some of the cases before ileosigmoidostomy. The result of the fat balance test in Case 2, following ileosigmoidostomy, our best case so far, is disappointing—77 per cent fat absorption. (Normal fat absorption is 90 per cent and above.) This disappointing result is difficult to explain in view of the excellent clinical result. His bowel motions were reduced from 8 to 2 per day immediately after operation and they became of normal appearance. It is perhaps likely that there was an error in carrying out the test. The test requires very careful supervision from beginning to end to ensure that the patient gets only the diet prescribed for him and that all specimens of feces for the 3 day period of collection are saved. Breakdown is very likely and has necessitated the restarting of the test in some of our other cases. This patient should have had the fat balance test repeated. It is very unfortunate that this was not done. It is doubly unfortunate that he would not submit to investigation when last seen in 1952, as we are convinced that he would have shown fat absorption well within the limits of normal.

In Case 3, the elderly infirm patient showed a fat absorption of 90 per cent, a low normal, and very satisfactory in view of his slightly disappointing number of bowel motions per day. In Case 4, the only other patient whose record of fat absorption following ileosigmoidostomy is available shows a fat absorption slightly below normal, but he is obviously not suffering in health as a result of this slightly deficient bowel absorption.

The results of the fat balance test indicate that there is sometimes a slight degree of deficient intestinal absorption following ileosigmoidostomy.

Fecal fat estimations were carried out in some of the cases following ileosigmoidostomy. The fat content and proportion of unsplit fat were higher than normal. Attention is drawn to our previous remarks about the value of this test; only single estimations were carried out. However, a moderately high result would be expected in the presence of a mild degree of intestinal hurry.

All other investigations (listed in the case reports) have revealed no evidence of a deficiency state and, where preoperative and postoperative estimations are available for comparison, normality returns following operation when abnormality had been recorded prior to operation. From the results it can be concluded that the slightly deficient intestinal absorption which may remain following ileosigmoidostomy is of no importance. This conclusion is also supported by the excellent state of nutrition found on ordinary clinical examination.

Intestinal hurry was also investigated by means of barium meal and follow through radiologic examination in Cases 3, 4, 5, and 6. In Case 3 intestinal hurry was evident from the history of 2 to 4 loose bowel motions per day and the presence of numerous undigested muscle fibers in the stools. The barium series confirmed the presence of intestinal hurry. A trace of barium appeared in the sigmoid at 3 hours, and at 5 hours the sigmoid was well defined with barium. This case showed the fastest passage from stomach to sigmoid. In Case 4 the sigmoid had filled in 7 hours, which is possibly near normal. Case 6, following ileosigmoidostomy and before further operative intervention, showed no evidence of intestinal hurry. No barium had appeared in the sigmoid at 6 hours; it had by then reached the distal ileum. The result in Case 5 is of little significance, as the fistula had been closed when the barium meal and follow through examination was performed, but it perhaps indicates that the normal rate from stomach to sigmoid is about 7 hours and serves as a control for the other cases. In a patient with a normal small bowel, the time taken for

barium to reach the cecum is 7 to 10 hours. The only case, then, which shows definite radiologic evidence of intestinal hurry, following ileosigmoidostomy, is Case 3.

In 3 of the 4 patients who had barium meal and follow through examinations following ileosigmoidostomy an interesting observation was made. Once the sigmoid had filled, there appeared to be retrograde movement from the sigmoid to the descending colon. This observation suggests that the sigmoid and descending colon are used as a reservoir for feces and helps to explain the infrequency of motions in most patients with an ileosigmoidostomy. It is also suggested that by this means some absorption of water may occur from the large bowel and so lead to a more solid consistency of the intestinal contents before defecation. It thus is evident that, in spite of ileosigmoidostomy, the function of the large bowel is, partly at least, preserved.

Although ileosigmoidostomy diverts the fecal stream from cecum, ascending colon, transverse, and descending colon direct to the sigmoid, it is rather remarkable that this should make such a difference to the number of motions per day, abolish vomiting, and lead to such great improvement in the general condition when some of our findings are considered. First of all, it is quite obvious that feces must pass in retrograde fashion up the descending colon, as did the barium on follow through examination, and some must reach the level of the fistula. Again, in Case 5, it was found that the ascending colon contained fresh feces and succinylsulfathiazole, given preoperatively, at the operation to restore the normal anatomy of the bowel. In Cases 4 and 6, the ascending colon, on straight x-ray film, was seen to be filled with fecal material. In most cases, then, feces must reach the level of the fistula and probably pass beyond it. Why do feces not pass through the fistula and keep up the jejunitis and intestinal hurry? It is possibly due to the fact that less feces are passing the fistula than normally and perhaps these feces are of a more solid nature than before operation. However, it seems likely that feces will sometimes pass through fistula to stomach and jejunum. Intestinal hurry is greatly reduced but not usually completely abolished by ileosigmoidostomy. Closure of the fistula (Cases 1, 5, and 6) abolishes intestinal hurry completely. It is suggested therefore, that, although no fecal material or smell may be detected during fractional test meal after ileosigmoidostomy, occasionally very small quantities of feces pass through into stomach and jejunum and so keep up a very mild jejunitis. This was shown to happen in Case 2. In the fractional test meal flecks of feces were seen in some of the specimens. This would explain the very slight degree of intestinal hurry which is often still evident after ileosigmoidostomy. That some degree of intestinal hurry is present and that the increased number of bowel motions is not due to short circuiting the large bowel is proved by the result of closing the fistula in the patients in Cases 1, 5, and 6, who still have ileosigmoidostomies.

When partial gastrectomy followed ileosigmoidostomy in this series, the large bowel was not resected. The transverse colon was separated from the fistula and the resulting gap in the colon repaired. Lahey, on the other hand, at the second operation resects the terminal ileum, cecum, ascending colon, and transverse colon to a point just beyond the fistula, in addition to carrying out partial gastrectomy. Lahey leaves a short blind loop of colon, but in the above operations a long blind loop is left. In 1 of our patients (Case 4) stagnation of feces in the blind loop appeared to be proved. During barium meal and follow through examination, it was noted that cecum and ascending colon were filled with fecal material plus a little barium from the barium enema carried out 30 days previously. This appeared to remain quite static throughout the examination. This finding caused some concern. It showed the possible danger of stagnation of feces in the blind loop and it was decided to keep a careful watch on this after the patient was discharged from hospital. Since then, periodic straight x-ray

film of the abdomen has shown that feces remain in the ascending colon, but the amount varies, indicating that although movement of bowel contents here may be slow, there is certainly no real stagnation. In addition, the patient remains in good health over 5 years after operation. In view of this finding in Case 4, the other patients were checked by straight x-ray film of the abdomen and in none was there evidence of stagnation of feces in the ascending colon, although 1 (Case 6) showed a fairly large amount of feces in the cecum and ascending colon. In the only case in which it was decided to restore the normal continuity of the bowel (Case 5) fresh feces and succinylsulfathiazole given preoperatively were present in the cecum, and there was no dilatation of the cecum. In view of these findings at operation, it was doubted whether the abdominal pain, of which he complained and which led to operation, was really caused by back pressure in the blind loop. Being wise after the event, it would have been better to leave his bowel as it was.

We do not consider that leaving the long blind loop of colon constitutes any danger to the patient. On the contrary, its retention may be of value in that the absorptive capacity of the large bowel is retained. It follows that we are of the opinion that the Lahey colectomy may be unnecessary and only adds time to an operation, which, without colectomy, is a severe strain on the patient.

Far from favoring colectomy, not only did we think that the large bowel should be left intact but also we had been seriously considering the advisability of restoring the normal continuity of the bowel in our gastrectomized patients until the fatal outcome of this operation in Case 5 gave us cause to doubt the wisdom of such an undertaking. It was a reminder that such an operation is a major procedure accompanied by considerable risk even in these days of antibiotic cover. Until this accident, no definite decision had been reached as to whether all patients submitted to partial gastrectomy should have a further operation to restore normal bowel continuity. Now we have no doubt that the correct treatment is to leave these patients alone. They have no symptoms attributable to the presence of an ileosigmoidostomy—we believe now that this could also be said of Case 5 and so the only reason for restoring the normal continuity of the bowel would be an undue preoccupation with seeing the normal anatomy restored, surely a quite unjustifiable reason for subjecting patients to considerable operative risk. Stagnation in or back pressure in the blind loop of colon might have been held as an adequate reason for further operation, but, as we now consider that this danger is negligible, if not nonexistent, no argument can be made for restoration of normal bowel continuity.

In Case 5 at the operation for restoration of normal continuity of the bowel, it was noted that there was gross dilatation of the blind loop of ileum at the ileosigmoid anastomosis and that the stoma itself had stretched to 3 to 4 inches in length. When partial gastrectomy was carried out in Case 6, the ileosigmoid anastomosis was inspected because of the findings in Case 5, and again it was noted that the blind loop of ileum was somewhat dilated. In this case, however, the dilatation was not nearly so marked, but this may have been due to the fact that the ileosigmoidostomy had not been present for such a long time. This dilatation is a potential danger to the patient. It would probably be much better to use a lateral type of anastomosis including the end of the ileum in the stoma, in an attempt to prevent this tendency to dilatation of the blind loop which may occur with a side-to-side ileosigmoid anastomosis. On the other hand, an antiperistaltic anastomosis may be the answer to this problem. Lahey's anastomosis is antiperistaltic and it may be that the distal ileum is less liable to dilatation after an antiperistaltic side-to-side anastomosis.

SUMMARY

A series of 6 cases of gastrojejunocolic fistula treated by ileosigmoidostomy is pre-

sented. In the first case, ileosigmoidostomy was followed by partial gastrectomy and closure of the fistula, more or less following Lahey's regimen, except that the large bowel was not sacrificed. Subsequent patients were only subjected to partial gastrectomy if symptoms developed showing that further operative treatment was required. Of these 5 patients, 2 required partial gastrectomy with closure of the fistula because of the recurrence of peptic ulcer symptoms. In no case was it necessary to carry out further operative treatment subsequent to the ileosigmoidostomy merely because of the continued presence of the gastrojejunocolic fistula.

It is considered that the second operation may well be neither necessary nor desirable but that sometimes a second operation is required. The investigations and argument in support of this contention are presented.

We are of the opinion that the indications for partial gastrectomy and closure of the fistula after ileosigmoidostomy are: (1) the onset of dyspeptic symptoms indicating further peptic ulceration; (2) the patient whose symptoms due to his gastrojejunocolic fistula are not adequately controlled by ileosigmoidostomy.

We consider that the contraindications to partial gastrectomy and closure of the fistula after ileosigmoidostomy are as follows: (1) the elderly or unfit patient; (The only indication for further operative treatment in the elderly or unfit is the occurrence of dyspeptic symptoms causing worry to patient and doctor, which cannot be controlled by dietetic measures.) (2) the patient whose symptoms are completely cured by ileosigmoidostomy and who has no complaint of indigestion.

Ileosigmoidostomy is favored by us in the treatment of gastrojejunocolic fistula because: (1) It makes the patient fit for partial gastrectomy and closure of the fistula if this requires to be done. (2) It is a simple operation. (3) It may produce sufficient alleviation of symptoms as to make further operation unnecessary. (4) It is an ideal operation in the old and infirm as, in all probability, it will not have to be followed by partial gastrectomy.

However, in the few patients whose general condition permits it, we still believe that the operation of choice is partial gastrectomy and closure of the fistula in one stage.

The results of extensive investigations carried out on this series of patients are given and discussed. Following ileosigmoidostomy, the following abnormalities only have been discovered: (1) very slight degree of intestinal hurry except in 1 patient who appeared quite normal; (2) very slightly deficient intestinal absorption; (3) undigested food in the stool in 1 case, the elderly and unfit patient; (4) high fat content of stools.

These findings were not marked enough to cause any concern. All other investigations revealed normal results.

The operative technique and difficulties and complications encountered are discussed. It is suggested that the large bowel need not be sacrificed at the second operation and that its preservation probably serves a useful purpose. To avoid the dilatation of the blind loop of ileum at the ileosigmoid anastomosis it is recommended that a modified type of side-to-side anastomosis be employed. Reconstruction of the normal anatomy of the bowel is considered to be unjustifiable and dangerous.

In conclusion, ileosigmoidostomy is considered to be an excellent operation in cases of gastrojejunocolic fistula, either as a first stage procedure or as the one and only operation, when one stage obliteration of the fistula with partial gastrectomy is not possible.

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THE NUTRITIONAL STATUS OF PATIENTS AFTER PARTIAL GASTRECTOMY WITH GASTROJEJUNOSTOMY FOR DUODENAL ULCER

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THIS REPORT deals principally with the nutritional results which followed elective partial gastrectomy for peptic ulcer, with particular reference to the amount of stomach removed. Emergency gastrectomies are not included. It covers 1,068 patients, all of whom had duodenal ulcers, except 7 patients with jejunal and 7 with gastric ulcers who are included in a special group that underwent vagectomy[1] as well as gastrectomy.

As of January 1, 1955, we were currently in touch with 925 of these patients, 118 others had been followed until death, and the remaining 25 (2.3 per cent) had been lost to follow-up after an average of 4 years. The length of follow-up was from 2 to 19 years.

In 1953, we reviewed (2) the results following partial gastrectomy in 898 patients who had gastric or duodenal ulcers or both, and who were operated on during the period between 1936 and 1950. We have again reviewed and brought up to date the records of the patients in this group who had duodenal ulcers and added the patients who were operated on from 1951 to 1953. Some of these patients had a gastric ulcer in addition to their duodenal ulcer. The essence of our experience during the period from 1936 to 1953 was as follows: (1) over the years our surgical management improved, i.e., there were fewer postoperative deaths and late obstructions, infections, and hernias in the latter part of the period than in the earlier; (2) higher resections apparently were done in the later years than in the earlier; (3) the results of the shift to higher resections appeared to show little, if any, improvement in the incidence of marginal (jejunal) ulcers and to demonstrate a definite increase in the incidence of dumping and nutritional problems. Whereas, prior to 1945, dumping and nutritional problems after operation were a rarity, after 1948 they became commonplace.

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[1]The term "vagectomy" is used here to mean usually removal of a portion of the right and left vagus trunks, although sometimes the nerves were simply divided.

SIZE OF RESECTED SPECIMENS

As with other clinics, prior to 1953 our causes for dissatisfaction with our operative results fell into two main categories, namely, the recurrent ulcers and the nutritional-dumping problems. It appeared that the latter increased in number as we increased the proportion of stomach that was habitually resected. As proof, we had first to show that higher resections had in fact been performed in the years when the dumping and nutritional problems were most numerous. The surgeon's estimate of the proportion of stomach that was removed, even if stated in the operative report, was unreliable. As a measure of the amount of stomach removed we took instead the length of the resected specimens along the greater curvature as recorded in the pathologic reports. In comparing two stomachs to find the proportion of each removed, this single measurement would be of little value, but, in comparing groups of several hundred stomachs with each other, any striking difference in this measurement among the groups would be significant in determining which patients on the average underwent higher resections.

TABLE I.—SIZE OF PORTIONS OF STOMACH RESECTED FOR DUODENAL ULCER ACCORDING TO YEARS OF OPERATION

	1936 to 1948		*1949 to 1953*	
No. of patients who survived operation	486		462	
Estimated usual amount of stomach removed, per cent	50		60–75	
Per cent of specimens, according to length along greater curvature				
0 to 18 cm.	47	77	20	
19 to 22 cm.	30		39	80
23 cm. plus	23		41	
Marginal ulcers proved or suspected, per cent	7.8		6.3*	

*Shorter follow-up period than for the 1936 to 1948 group. The marginal ulcers occurred in the 0 to 18 cm. group at the rate of 8 per cent, in the 19 to 22 cm. group at 7.3 per cent, in the 23 cm. plus group at 5.1 per cent.

TABLE II.—SIGNIFICANT NUTRITIONAL AND DUMPING PROBLEMS AFTER RESECTIONS WITHOUT VAGECTOMY*

	1936 to 1948	*1949 to 1953*
No. of patients who survived operation	486	462
Estimated usual amount of stomach resected, per cent	50	60–75
Per cent of patients who lost 5 per cent of preop. weight in 3 yrs.	14	31
Patients with clinically disturbing weight loss, per cent	2.1	11.9
Patients with serious postop. nutritional defects, per cent	1.6	6.3
Patients noted to have dumping, per cent	9	27

*Omitting patients with serious complicating disease other than ulcer, except in the "dumping noted" column.

The measurements are recorded in Table I, which indicates that a larger proportion of the stomach was habitually removed during the years between 1949 and 1953 than prior to 1948. Although included in the tables with the earlier years, 1948 was a transitional year when we were changing over from low resections, chiefly of the Polya type and usually done through a transverse upper abdominal incision, to high resections of the Hofmeister type, nearly always done through a vertical upper midline incision to permit access to the upper half of the stomach.

RELATION OF NUTRITION TO SIZE OF RESECTION

The next problem was to relate the state of nutrition of the patients after operation to the extent of the resections. For the purpose of comparing the state of nutrition of patients with high and low resection, we determined for all of them the answers to the following questions, viz., (1) which patients within the first 3 years after operation lost 5 per cent or more of their preoperative weight, (2) which patients after operation suffered a clinically disturbing weight loss, (3) which patients developed nutritional problems after operation that needed medical attention? In the first question, the period of 3 years was chosen so that the recent cases could be fairly compared with the earlier. The period of follow-up must be the same for the groups compared because many patients who lost weight shortly after operation experienced a gain about 5 years later. In the second question, the word "disturbing" was interpreted in terms of the patient's need to gain. Patients frequently come to operation overweight because of the diet that they have been forced to take to control their pain. A loss of weight from 200 pounds to 170 after operation would not be disturbing, but a drop from 100 to 95 might well be (Table II).

By all of these standards the result was the same. The resections done during the period from 1949 to 1953, i.e., those of more than 50 per cent, clearly led to more dumping and nutritional problems than did the smaller resections. They led, it is true, to many weight losses which clinically were not harmful and at times even beneficial, but in too many instances they were followed by persistent dumping and underweight of serious proportions.

ESTIMATION OF PROPORTION OF STOMACH REMOVED

How do we know that the specimens of stomach removed during the period from 1936 to 1947 represented approximately 50 per cent resections? In 1952, following the publication of the work of D. A. Farmer and his associates(1, 3) we began subjecting a series of patients to resection plus subdiaphragmatic vagectomy, hoping in this way to reduce the number of marginal ulcers that followed resection alone. During

1952 and 1953 we continued to do high resections when we did the vagectomies, but thereafter a deliberate effort was made to avoid removal of more than half the stomach. The cases with vagectomy therefore fall into two groups, one with high resection and the other with low. Our method of measurement of the stomach at operation was inexact but practical. After the lower half of the stomach was freed and the duodenum cut across, we allowed the stomach to lie without traction in the wound in approximately its normal position. A point was then selected on the greater curvature that was equidistant by straight line measurement from the pylorus and from the highest point on the fundus (this point is always at some distance from the esophagogastric junction). For purposes of measurement, the ordinary metal sucker tube worked well enough. A Payr clamp was placed across the stomach nearly transversely from the point so established on the greater curvature. By using the Payr clamp as a hinge, the lower portion of the stomach could then be superimposed upon the upper portion, with the pylorus lying on the highest point of the fundus. The two portions corresponded to each other well enough to demonstrate that the lower part of the stomach, which was to be removed, represented about 50 per cent or less of the whole stomach. It could certainly be shown that the lower part was not twice the size of the upper, which it would be if two-thirds of the stomach were being removed. For the purpose of this article, stomachs measured in this way before resection are classified in the 50 per cent resection group. When we carried out this simple maneuver and then measured the resected specimens in the laboratory, we found that the lengths along the greater curvature were similar to those of the 1936 to 1948 period and less than those of the 1949 to 1953 years (Tables I and III).

TABLE III.—SIZE OF PORTIONS OF STOMACHS RESECTED, WITH VAGECTOMY, ACCORDING TO YEARS OF OPERATION

	1952 to 1953	*1954 to April 1956*
No. of patients	43	59
Estimated usual amount of stomach resected, per cent	60–75	50
Per cent of specimens, according to length along greater curvature		
0 to 18 cm.	15	47 } 80
19 to 22 cm.	40 } 82	33 }
23 cm. plus	42 }	20
No record	3	
No. of patients with persistent dumping after operation	6†	0
No. of patients with serious nutritional problems after operation*	2	0
No. of patients who developed probable marginal ulcer	1	1

*Omitting patients with serious complicating disease other than ulcer.
†2 serious.

EFFECT OF RAPID EMPTYING

One factor other than the size of the resected portion of stomach seems to be important in relation to the incidence of dumping. It is best described by giving an illustrative case.

S. W., a married female, aged 26 years, underwent a high resection as an emergency measure for acute massive hemorrhage in 1951. She weighed 105 pounds before operation. After operation she did poorly, largely because of severe persistent dumping. She also had psychiatric problems for which she received shock treatments in 1952. She was readmitted in November 1955 for revision of the gastrojejunostomy. Roentgenograms of the gastrointestinal tract before the revision showed that barium reached the midileum 10 minutes after she had swallowed it (Fig. 1). The afferent anastomotic jejunal loop approached the stomach from the lesser curvature side and the efferent limb descended from the stoma almost vertically, permitting extremely rapid transit of barium through the stomach into the small bowel. At the second operation the direction of the jejunal loop was reversed so that the afferent loop approached the greater curvature. Subsequently, it was seen that swallowed barium was directed from the stomach into the afferent loop and duodenum, from which it was ejected on past the stoma by peristaltic action little by little into the remainder of the small bowel (Fig. 2). The patient weighed 85 pounds shortly after the second operation. She has since gained and weighs 107 pounds. She still occasionally experiences sweating and palpitation after meals but no longer has severe symptoms of dumping unless she "drinks a lot of fluid fast." She has a small stomach and still vomits food promptly if she overeats, but this she usually can avoid doing. Her case does not resemble the afferent loop syndrome described by Jordan. She is working and eats a normal diet. Her psychoneurotic person-

FIG. 1. This roentgenogram of patient S. W. was taken with the patient supine 10 minutes after she had swallowed some barium mixture. It shows very rapid filling of most of the small intestine. The arrow points to a small amount of barium that entered the afferent jejunal loop as it approaches the lesser curvature. This study was done during the period when the patient was having severe symptoms of dumping after nearly all meals before revision of the gastrojejunostomy was done.

ality probably plays a part in her symptom complex, and the small size of her stomach has not been remedied.

This case is not cited as an explanation of the mechanism of all dumping or as an illustration of the way that all patients can be cured of dumping. It does illustrate an arrangement of the gastrojejunostomy (that done at the first operation) which should and can be avoided. We now usually run the anastomotic jejunal loop from left to right, fastening the efferent loop upward along the lesser curvature of the gastric stump for about 2 to 3 centimeters. It is hard to know how important this maneuver is, but there has been no significant dumping among the patients who have undergone a 50 per cent resection plus this type of gastrojejunostomy, without regard to the size of the stoma.

NUTRITIONAL STATUS OF PATIENTS WITH VAGECTOMY

The state of nutrition of the 102 patients who had vagectomy with resection can be expressed not only in relation to the 948 patients who survived high or low resection without vagectomy but also in more nearly absolute terms, because the 102 patients' heights are all recorded. Their status can be summarized as follows: (1) Two patients (i.e., 2 per cent of the 102) have developed recurrent (jejunal) ulcers and possibly a third, although the evidence is against it. In 1 of the 2, the vagectomy probably was incomplete, as he had free hydrochloric acid in his gastric juice after operation. Both are now free of evidence of ulcer after a period of conservative therapy. This record compares with 6 per cent of recurrent ulcers that developed among the patients who had high resections without vagectomy after the same length of follow-up. (2) Immediate and late undesirable side effects attributable to the vagectomy have been unimportant, except in 1 patient with postoperative paralytic ileus that lasted 8 days and 1 patient who appeared to have spasm of the efferent jejunal loop for 3 months after operation. Both patients recovered fully. Cramps and diarrhea in the late postoperative period have so far not been frequent or serious. Temporary distention and looseness of the bowels have been observed in about 10 per cent of the cases. (3) All of the patients have returned to their customary work or activity. (4) Dumping has been eliminated as a complication of clinical importance. Among the 43 patients who underwent vagectomy plus high resection, 2 have persistent dumping of distressing degree, 2 of intermediate degree, and 3 of minimal degree, but among the 58 survivors with vagectomy plus 50 per cent resection there are none who have had more than mild and temporary dumping symptoms and only 10 who have had even this degree of it. (5) The appraisal of the post-

operative nutritional status of patients cannot be based on any one standard. We have checked the weights of the resection plus vagectomy group against a table of average weight for height, age, and sex which was prepared by The Equitable Life Assurance Society of the United States, based on 60,000 purchasers of life insurance in 1940. Average weight does not imply optimal weight; in the United States it may well be above optimum. We are informed that it is the practice of life insurance companies to allow weights as low as 25 per cent below the average, without imposing higher than normal premiums upon applicants for insurance because of their being underweight, i.e., the insurance companies have not found that this degree of under average weight constitutes a sign of life expectancy appreciably shorter than average. If a disease is found to accompany the under average weight, then the disease is considered in setting the premium.

We have established the following facts about the 102 patients who underwent partial gastrectomy with vagectomy. (1) Thirty-seven are now of average weight or above, 49 are less than 20 per cent below average weight, 15 are more than 20 per cent below average. There was 1 postoperative death. Of the 15 more than 20 per cent below average, 11 have good reasons other than the gastrectomy for being so, such as malignant tumor, severe rheumatoid arthritis, severe psychoses, and alcoholism; the other 4 of the 15 are all working, although 2 of them, who had high resections, are somewhat handicapped by being underweight. (2) There are 7 of these 15 patients who after operation are more than 25 per cent below average weight, and so might constitute poorer than average life insurance risks because of their state of nutrition. All but 1 of these has concurrent disease other than ulcer adequate to explain the under average weight. The other one has always been lean and is now apparently in good health and working. (3) The total of 64 per cent of patients who are under average weight after operation is to be compared to a little over 50 per cent found by the Equitable Life Assurance Society among their applicants for insurance. Fifteen of the 64 per cent have diseases other than ulcer that could explain their being under average weight. Of the patients whose health is uncomplicated by serious disease other than ulcer, 37 (43 per cent) after operation are of average weight or above and 49 (57 per cent) are under average. (4) Of 64 patients now below average weight, all of those more than 20 per cent below and all but 6 less than 20 per cent below were below average weight before operation. (5) Two of the 102 patients

FIG. 2. This roentgenogram was taken with the patient S. W. erect about a half hour after she had swallowed some barium mixture. The gastrojejunostomy has been revised so that the afferent jejunal loop now approaches the greater curvature side, running past the stoma to the lesser curvature where it is fastened up along the stomach wall for about 4 centimeters. Arrows point to the afferent jejunum and duodenum which are filled with barium from the stomach, some of which has gradually gone over into the proximal jejunal loops beyond the stoma. Symptoms of dumping have markedly diminished and she has gained 20 pounds from her low weight, but her stomach is small and she must eat small meals.

with vagectomy and resection appear to be limited in their activity or enjoyment of life by their nutritional status alone, i.e., they have no complicating disease to explain their limitations, and 2 others by persistent symptoms of dumping. All 4 of these patients were operated on in the years when high resections were being done. None of the patients with vagectomy and 50 per cent resection are so handicapped. (6) Only 2 patients have been referred to the medical clinic after operation, one because of pain from a marginal ulcer and the other because of dumping. Both of these were in the high resection group. In the 50 per cent resection group, no nutritional problems have arisen that required medical consultation.

DISCUSSION

It is evident that in our experience resections of more than half of the stomach for duodenal ulcer were followed by an appreciable morbidity due to malnutrition and dumping, whereas resections of about 50 per cent of the stomach, whether accompanied by vagectomy or not, caused few of these difficulties. High resections afforded little if any benefit in lowering the incidence of marginal ulcers as compared to 50 per cent resections. The addition of vagectomy to 50 per cent resection lowered the incidence of marginal ulcers and caused few disagreeable side effects. This is in agreement with most of the reports published from other clinics. The scarcity of significant dumping after 50 per cent resection is a strong point in its favor. The state of nutrition of patients after 50 per cent resection with gastrojejunostomy, with or without vagectomy, is so satisfactory that in my opinion there is no need for introducing other procedures, such as the Billroth I operation, except perhaps in a few exceptional cases.

The validity of this appraisal of the state of nutrition of the patients with vagectomy, gastric resection, and gastrojejunostomy depends largely upon how fairly the patients with severe concomitant disease other than ulcer have been evaluated. The operation cannot be expected to offset the effects of alcoholism, psychoneuroses, or other debilitating diseases that complicate the ulcer. On the other hand, the appraiser must not assume that mild degrees of these conditions explain all cases of postoperative malnutrition. Inasmuch as we claim no originality for any operative procedure for ulcer, we can hope that we have succeeded in being objective in appraising the operative results.

CONCLUSIONS

1. Gastric resections of more than 50 per cent for duodenal ulcers should not be done, except perhaps in exceptional cases.

2. The addition of vagectomy to 50 per cent resection results in a lowering of the incidence of marginal ulcers compared to that which follows even higher resections without vagectomy.

3. The nutritional status of patients after 50 per cent gastric resection with gastrojejunostomy and vagectomy has been satisfactory in our experience unless the patient had a complicating disease that in itself could cause malnutrition.

4. The highest proportion of satisfactory results in our experience in treating duodenal ulcers has followed resection of about 50 per cent of the stomach, with gastrojejunostomy and vagectomy and avoidance of abrupt descent of the efferent jejunal limb from the stoma. A further period of careful follow-up observation of the patients who have undergone this type of operation is needed to substantiate our present impression.

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EXPERIMENTAL USE OF HOMOLOGOUS FASCIA LATA TO REPAIR DIAPHRAGMATIC DEFECTS IN DOGS

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ALTHOUGH DIAPHRAGMATIC HERNIAS can usually be repaired by approximation of the edges of the defect, not all can be treated in this way.

Large defects in the diaphragm may be due to congenital or traumatic causes or to recurrent hernias. They also may be left by necrosis following infection or by extensive resection of the diaphragm in continuity with a neoplasm. In some patients, a means of closing large defects other than suturing the approximated edges must be devised.

Three general types of procedures have been used to accomplish closure of large diaphragmatic defects. One is by releasing tension on the diaphragm peripherally to allow approximation of the edges of the defect without undue tension. This release has been accomplished by preliminary extrapleural thoracoplasty, resection of small segments of ribs, and elevation of the attachment of the diaphragm.

The second type of repair includes the use of nearby structures to close the opening. These include renal fascia, latissimus dorsi muscle, and a lobe of the liver.

The third procedure makes use of a patch of a wide variety of materials. Among these are metallic mesh, cutis grafts, autogenous fascia lata, and preserved homologous fascia lata, lyophilized or preserved in antihistamine solution. The presence of metallic mesh near the esophagus and aorta and the abscesses and granulomas associated in some instances with cutis grafts are real objections to these materials. The experimental work with preserved homologous grafts of fascia lata has not been completely convincing.

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Having in mind large diaphragmatic defects in the newborn in whom the removal of fascia lata for an autologous graft would add undesirable trauma or hazard as would the use of renal fascia, latissimus dorsi muscle, or the liver, we considered the use of a fascia lata patch obtained from one of the parents as a possibility. A review of the literature discloses no study of the use of fresh homologous fascia lata in repairing large diaphragmatic defects. As a basis for possible justification of its use in repairing diaphragmatic defects in man, we undertook the following investigation.

METHODS AND MATERIALS

Twenty-one adult mongrel dogs weighing from 9 to 14 kilograms were used. Diaphragmatic defects were repaired in 14 dogs. Fresh homologous fascia lata was obtained from one thigh of 6 and both thighs of 4 dogs used as donors. Three donors later received grafts of homologous fascia lata.

Intraperitoneal injection of pentobarbital sodium in amounts of 27 milligrams per kilogram provided the anesthesia. Respirations were maintained by intermittent insufflation of room air through an endotracheal tube. After the skin of the donor animal had been suitably prepared, all the fascia lata available was removed through a longitudinal incision in the thigh. The fascia lata was placed in a surgical sponge moistened with saline solution while the incision in the donor animal was closed.

The left thoracic cavity of the recipient animal was approached through the bed of the tenth rib. The central tendon of the left hemidiaphragm was excised as was part of the muscular portion. There remained a border of about ½ centimeter medially and

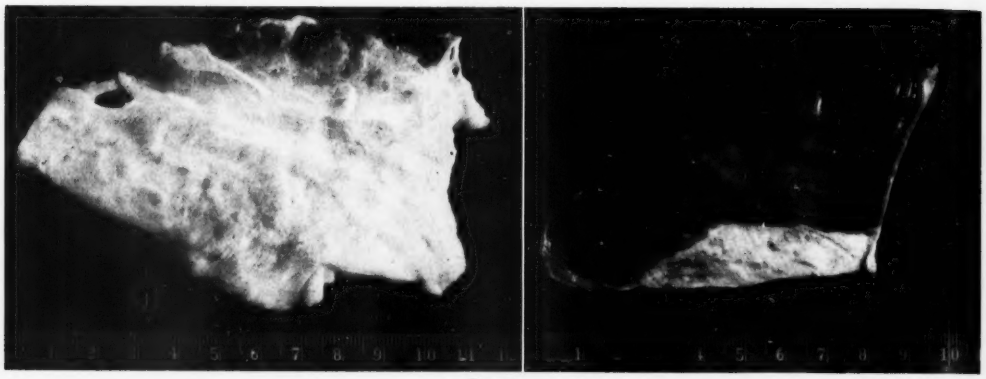

FIG. 1.

FIG. 2.

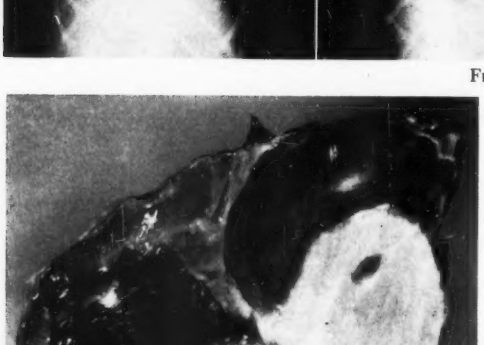

FIG. 3.

FIG. 1. a, The fresh fascia lata homograft used to patch the defect. b, A representation segment of the diaphragm excised for creation of the defect.

FIG. 2. Intact diaphragm with normal curvature.

FIG. 3. The gross appearance of the left hemidiaphragm removed at necropsy 2 weeks after insertion.

1 centimeter along the costal margin. The average defect measured 5 by 7.5 centimeters. Figure 1 shows the excised segment of diaphragm and the fascia lata homograft to be used in the repair of the resulting defect. The graft, trimmed to fit the defect, was held in place with interrupted fine cotton sutures which imbricated the edges. The lung was re-expanded, and the chest was closed in layers without drainage. Approximately 1 hour elapsed between the time the graft was obtained and its installation in the recipient animal. No antibiotics were used. All animals survived.

The animals were active in the postoperative period and presented no abnormalities on physical examination. Skin disorders were noted in 2 animals. Roentgenograms in 5 animals revealed no deformity of the diaphragm (Fig. 2). The animals were sacrificed 2 at a time, ½, 1, 2, 4, 6, 10, and 12

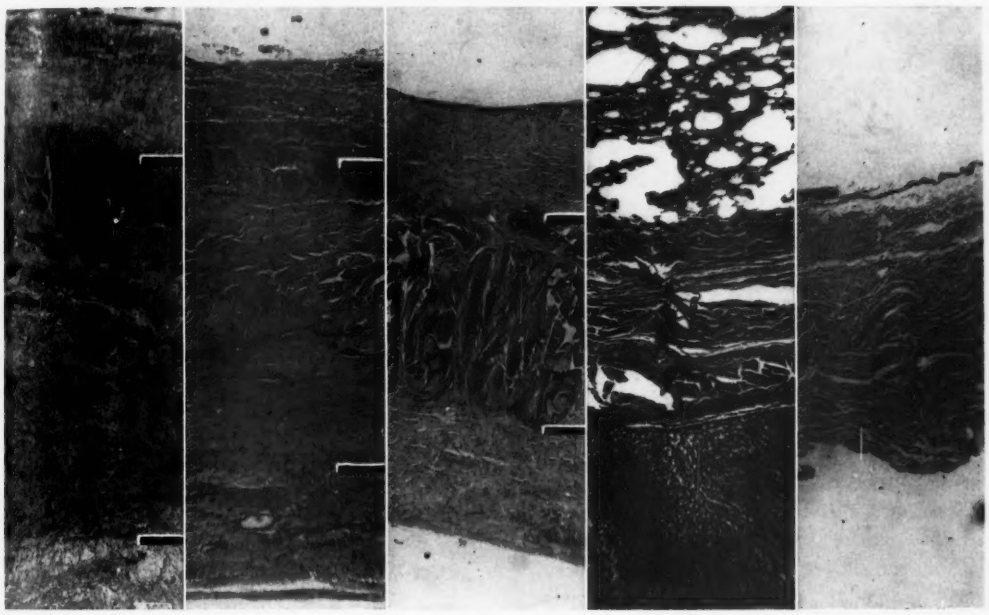

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FIG. 4. Photomicrographs of the fascia lata homografts removed at necropsy (all magnified 40 times). a, Two weeks after insertion. The area of the homograft is the central two-thirds of this photomicrograph that is darker than the rest. The upper and lower surfaces of the graft are covered with fibrin from the host. All tissues are infiltrated with round cells. b, Less edema and round cell infiltration than noted in (a). The round cell infiltration is most perivascular. c, Two months after insertion. Less edema than noted in (b). The host's fibrous reaction now consists principally of collagen bundles. d, Four months after insertion. The lung above and liver below are adherent to the homograft in the central part of the photomicrograph by the host's fibrous reaction. The homograft at this time resembles normal fascia and cannot be distinguished from the tissue reaction of the host. e, Twelve months after insertion. The host's fibrin reaction and the homograft cannot be identified as separate tissues.

months subsequent to the insertion of the graft.

The gross appearance of the homografts and patches of fresh fascia lata examined at necropsy 2 weeks after their insertion manifested considerable inflammatory reaction (Fig. 3). The grafts were red, thick, firm, and lightly adherent to adjacent viscera; the silvery collagenous bundles normally visible were obscured. Microscopic examination (Fig. 4a) revealed both surfaces of the graft to be covered with fibrin from the host infiltrated with round cells. The graft was edematous and also was infiltrated with round cells. Higher magnification revealed degenerating fibroblasts in the fascial graft and early organization of the host's fibrinous reaction.

The homografts observed 1 month after their transplantation had less inflammatory reaction than those which had been in place for only 2 weeks. The month old grafts were light gray, thick, firm, and partially adherent to adjacent viscera. Their microscopic appearance (Fig. 4b) disclosed less edema and fewer inflammatory cells, most of which were in perivascular spaces. Higher magnification revealed early ingrowth of fibroblasts in the graft and complete organization of the fibrin.

The homografts examined 2 months after their transplantation showed still less evidence of inflammatory reaction. They were somewhat thicker and denser than normal fascia lata but this change was much less than that found in the grafts removed at earlier necropsies. The silvery collagenous

bundles could be seen in the parts of the graft not covered by adhesions. On each side of the graft microscopic examination (Fig. 4c) disclosed quite dense collagenous fibers with small fibroblasts and a little perivascular infiltration with round cells.

The homografts examined 4 months after their transplantation were similar to normal fascia lata in thickness, consistency, and appearance. The silvery collagenous bundles were readily visible wherever the surface of the graft was free of adhesions. Microscopic examination (Fig. 4d) revealed the collagenous bundles on each side of the graft to be about the same density as the fascia lata homograft. The photomicrograph shows the lung and liver adherent to the homologous fascial graft by the host's fibrous tissues. There was very little evidence of inflammation. Upon higher magnification the fascia lata homograft had a uniform distribution of living fibrocytes. One of the animals sacrificed at this time had a serious skin disorder and had lost weight. The homograft in this animal was thin and bulged into his chest, similar to an eventration of the diaphragm. All the other homografts in this study healed solidly and remained intact for the entire period of observation.

The homografts examined 6, 10, and 12 months after their insertion closely resembled fascia lata. No inflammatory reaction was noted on microscopic examination (Fig. 4e) except that usually found in the immediate vicinity of nonabsorbable sutures. Higher magnification of the homograft and the host's adjacent tissue revealed them to be of equal density and to have about an equal number of living fibrocytes. The differentiation between the former homograft and the host tissues was difficult if possible at all.

Measurement disclosed the average amount of shrinkage for all grafts was 20 per cent. Adhesions were noted between adjacent viscera and the graft in almost all animals and between the anterior part of the incision in the chest wall and the homograft in 5 animals.

SUMMARY

Fresh homologous fascia lata was used to repair large diaphragmatic defects in dogs. Gross and microscopic studies of the grafts were obtained at necropsies performed at intervals during the observation period of 1 year.

A subacute inflammatory reaction was present in the grafts that were in place a short time. This reaction was absent from the grafts examined 4 months or more after insertion. Although it remained intact, there was weakness in 1 homograft in an animal that had a skin disorder and had lost weight during the period of observation.

In the remaining 13 animals, the defects were soundly closed by the homografts which showed microscopic structure similar to the original fascia lata at the end of 4 months and later.

On the basis of these experiments, it would seem reasonable to use fresh patches of fascia lata homografts to repair large diaphragmatic defects in man, should the necessity arise.

TESTICULAR TUMORS IN INFANTS AND CHILDREN

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TESTICULAR TUMORS have received considerable attention in the surgical literature of the last few years, and large collected series of cases with follow-up data have been published; but there is little information concerning these lesions in infants and children. It is the purpose of this article to present our findings in a study of testicular tumors in infants and children seen at the Mayo Clinic, and to offer the results of a search of the literature in this field (11).

MATERIALS AND METHODS

Examination was made of the records of all children 14 years of age or younger whose condition was diagnosed at the Mayo Clinic between 1932 and 1952, inclusive, as malignant testicular tumor. Only those cases in which tissue was available were retained for study, and in all, 9 were collected thus. Routine histologic sections stained with hematoxylin and eosin were used throughout. When necessary, multiple sections and serial block sections of an entire lesion were studied.

CLASSIFICATION

Although the histogenesis of testicular tumors is not fully understood, the work of Friedman and Moore, Moore and Dixon, O'Connell and Geschickter, and others has provided a satisfactory histologic classification of these tumors. The recent versions recognize two well defined groups of testicular tumors, the germinal and the nongerminal. Constituting the germinal group are seminomas, teratomas, embryonal carcinomas, chorioepitheliomas, and combinations of these neoplasms. The nongerminal tumors of the testis are tumors similar to neoplasms which arise in other parts of the body. Interstitial cell tumors, androblastomas, and tumors arising from the rete testis are the only lesions in the nongerminal group which are specifically gonadal in origin.

In our series, 5 tumors were of the germinal type. Of these, 1 was a teratoma and 4 were embryonal carcinomas of the testis. The remaining 4 were classified as malignant neoplasms, probably sarcoma, and were considered to be in the nongerminal group.

THE GERMINAL TUMORS

Teratoma

CASE 1. In August 1950, at the age of 6 weeks, an infant was found to have a hydrocele in the left scrotal sac. During the ensuing 12 months progressive enlargement of the hydrocele was observed. At operation a testicular tumor was found in association with the hydrocele. Simple orchiectomy was performed, and the postoperative course was uneventful. Repeated follow-up examinations revealed that the patient had remained in good health for 4½ years following the initial treatment.

Pathologic examination revealed a tumor measuring 2 by 1 by 1.7 centimeters in the body of the testis. The tunica albuginea and epididymis were intact. The tumor appeared well circumscribed, and the cut surface was firm and grayish white with minute cystic spaces.

Histologically, the tumor was a teratoma made up of a mixture of well differentiated tissue, mainly cartilage, smooth muscle, and microcystic spaces lined by squamous and columnar epithelium of intestinal type (Fig. 1a). Serial block sections of the entire tumor revealed one narrowly limited region of small cell malignant tissue resembling neuroblastoma (Fig. 1b).

Embryonal Carcinoma

Case 2. In December 1950, the parents of a 12 month old boy observed that the infant's left testis was

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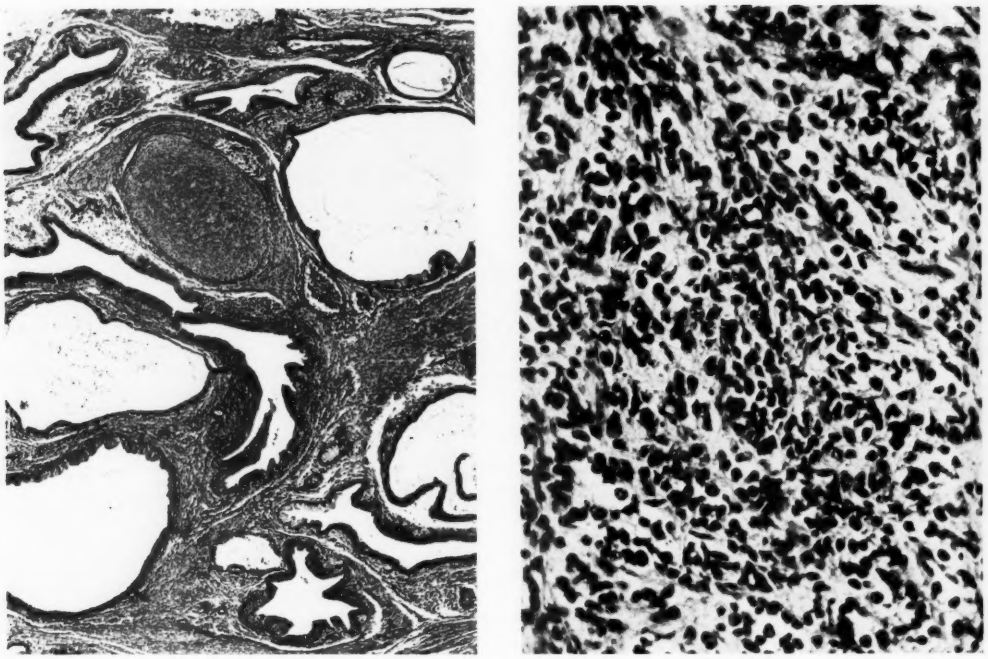

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FIG. 1. Case 1. Malignant teratoma. a, Histologic section showing teratomatous structure (×35). b, Small area of malignancy in one section (×300).

enlarged. Findings of physical examination were normal otherwise. A simple left orchiectomy was performed 1 month later, and radiation therapy was given postoperatively. In May 1951, during a routine postoperative checkup, a mass was palpable in the left flank. Roentgenologic examination revealed the mass in the left renal region, and an excretory urogram showed marked hydronephrosis of the left kidney. Shortly after the discovery of this mass, the child became irritable and refused his food; his condition deteriorated rapidly, and he died on May 30, 1951. Necropsy was not performed.

Histologic examination of this tumor revealed an embryonal carcinoma of glandular structure throughout, with extensive necrosis, hemorrhage, and occasional papillary infoldings (Fig. 2a).

CASE 3. The parents of a 17 month old boy noted a painless swelling of the left side of the child's scrotum. This enlargement persisted for 3 weeks before medical advice was sought. Physical examination revealed no other abnormality, except the mass in the left scrotal sac. At operation, a solid tumor of the testis was evident and left orchiectomy was performed. Radiation therapy was given postoperatively. The patient died 13 months later from the effects of widespread metastasis. Necropsy was not performed.

Histologic examination of the tissue removed at operation revealed an embryonal carcinoma which had broad sheets of large, anaplastic, epithelium-like cells with some differentiation into glandular spaces. Multiple large nucleoli, numerous mitotic figures, and zones of necrosis were present (Fig. 2b).

CASE 4. In June 1940, a 14 year old boy sustained an injury to his right testis. One month later, painless swelling of this injured testis was observed. Medical advice was not sought until December 1940. The results of the physical examination at this time were essentially normal, except for enlargement of the right testis, which was hard and as large as an apple. Simple orchiectomy was performed. During the postoperative period the patient received radiation therapy directed to his abdomen and lumbar region, and subsequently he was dismissed from the hospital. He was well until March 1941, when he complained of dull aching pain in the lower part of the abdomen. On physical examination at the clinic a mass with a diameter of 10 centimeters was detected in the suprapubic region. Further radiation therapy was administered to the abdomen, and improvement in his condition was noted. A few months later a roentgenogram of the thorax revealed metastatic lesions in the lungs. The patient's condition steadily deteriorated with gradual enlarge-

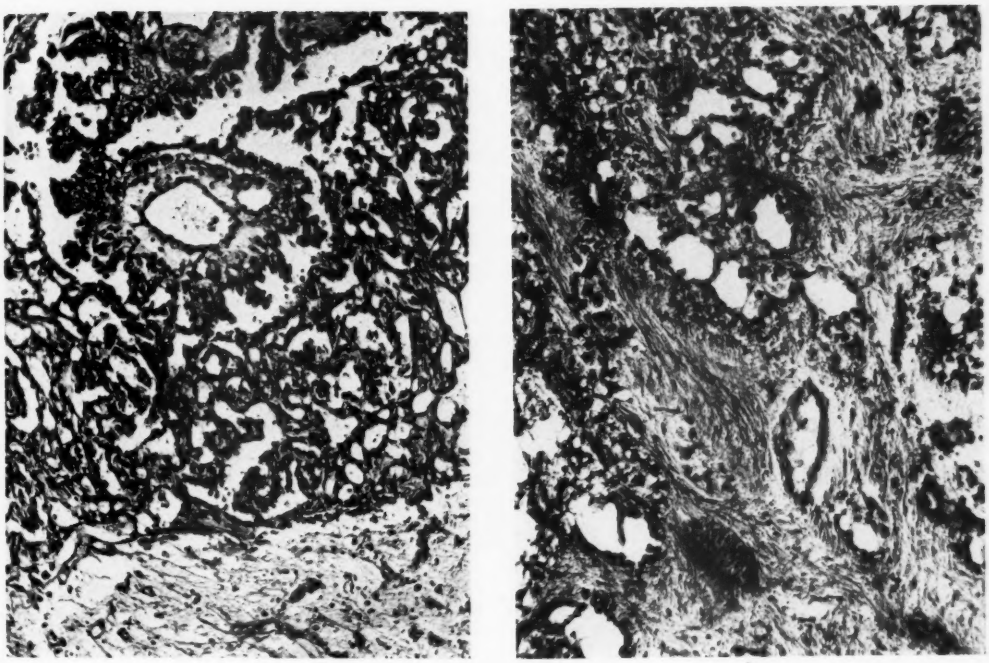

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FIG. 2. Embryonal carcinoma. a, Case 2. A reticulum-like pattern with papillary infoldings (×110). b, Case 3. Tendency toward glandular formation (×110).

ment of the abdomen, increase in the pulmonary metastasis, and the development of tumor tissue in the skin of the right lower leg. He died in August 1941.

Histologic examination revealed embryonal carcinoma of glandular type with much necrosis (Fig. 3a).

CASE 5. In a 13 year old boy who had been under medical observation since January 1943, because of fever of undetermined origin, a painless swelling of the left testis was observed in September of that year. Physical examination at the time revealed the presence of abdominal and inguinal masses in association with a hard, nodular tumor that filled the entire left scrotal sac. The boy was seen then at the clinic and was considered to be in the terminal stages of his disease. The only procedure performed was removal of a specimen from the left scrotal mass for examination. Death occurred shortly after the patient's return home.

Histologic examination revealed an embryonal carcinoma composed of large anaplastic epithelial cells with a slight tendency to gland formation (Fig. 3b).

THE NONGERMINAL TUMORS

CASE 6. A painless enlargement of the left side of the scrotum was noted in a 5 year old boy in May 1941. Approximately 2 weeks later this region was treated by radiation without benefit of biopsy. The patient was seen at the clinic in May 1932 because of continued enlargement of the scrotal mass. At physical examination, the scrotum was reddened and fixed to an enlarged, hard, tender testicular mass that measured 15 by 10 by 8 centimeters. Results of the remainder of the examination were normal. Simple orchiectomy was performed, and the patient received postoperative roentgenologic therapy directed to the lumbar and abdominal regions. A follow-up study disclosed that this patient was living and well 17 years later.

Histologic examination of this tumor revealed a spindle cell sarcoma apparently arising in the tunics of the testis. Multinucleated giant cells also were present (Fig. 4a).

CASE 7. A 6 year old boy first noted a painless swelling of the left part of the scrotum in April 1939. Medical treatment was not sought until October 1939, at which time a hard tumor about the size of a walnut occupied the left side of the scrotum. Other results of the physical examination were normal. Left simple orchiectomy was performed, and roentgen therapy was given postoperatively. The patient remained in good health until August 1940, when he complained of generalized abdominal discomfort. At physical examination a hard, nodular mass was felt

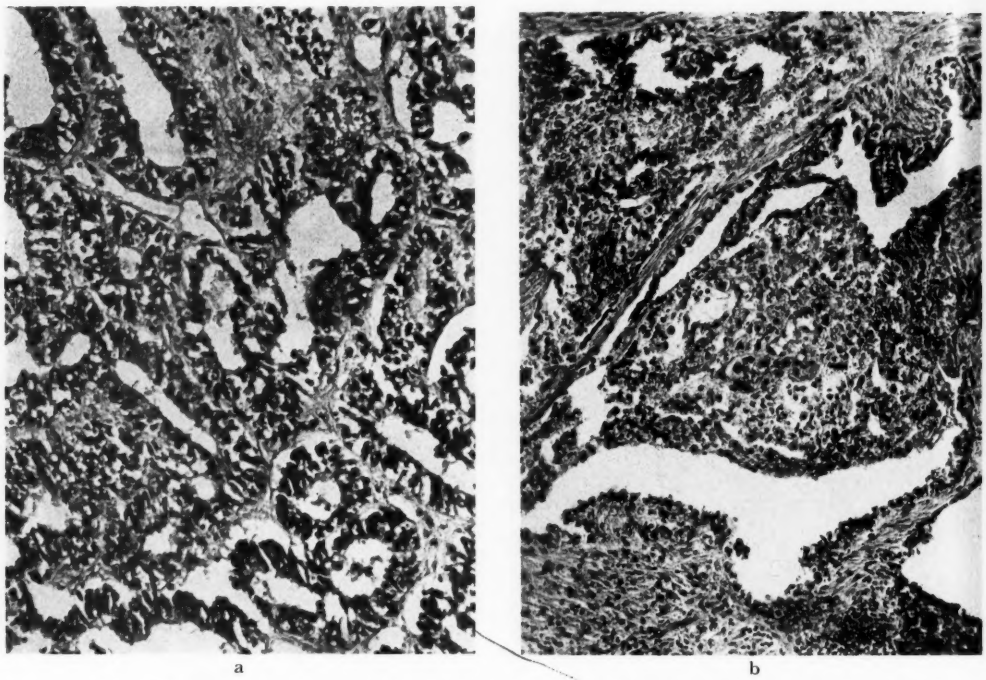

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FIG. 3. Embryonal carcinoma. a, Case 4. An unusual form of embryonal carcinoma exhibiting a marked degree of glandular differentiation (×180). b, Case 5. A pattern commonly seen in carcinoma of the testis in adults (×110).

in the left upper quadrant of the abdomen. The patient was seen shortly thereafter at the clinic, and was considered to be in a terminal phase. He returned to his home and succumbed in November 1940.

Histologic examination showed an undifferentiated spindle cell sarcoma which had infiltrated striated muscle. Elongated acidophilic cytoplasmic processes were present, and although cross-striations were not demonstrated, the tumor was considered to be a rhabdomyosarcoma (Fig. 4b).

CASE 8. In June 1940, a boy 7 years of age was found to have an enlargement on the left side of the scrotum. No other abnormalities were noted on physical examination. Two weeks later, simple orchiectomy was performed for a tumor of the testis. The patient was considered to be in good health until December 1940, when he complained of generalized abdominal distress. Physical examination at that time revealed a hard, tender mass measuring 8 by 8 centimeters low in the abdomen. Radiation therapy was directed to this region and symptoms were relieved. However, the clinical course was progressively downhill, and the child died from widespread metastasis in April 1941.

Histologic examination revealed a tumor pattern similar to that seen in Case 6. The tumor was found to involve the testicular tunics, and normal striated muscle fibers were seen in a number of sections (Fig. 5).

CASE 9. In February 1946, a 13 year old boy received a blow to his right testis. Considerable swelling and pain of the involved organ ensued from this trauma, and 2 weeks later surgical intervention was deemed necessary. At operation, a testicular neoplasm was discovered and simple orchiectomy was performed. The patient received roentgen therapy during the postoperative period. The boy enjoyed good health until June 1946, when his parents noticed that his appetite was poor and he complained of generalized abdominal discomfort. Physical examination revealed a tender, fixed upper abdominal mass, and he received further radiation therapy. However, his condition deteriorated rapidly; he died in August 1946.

Histologic examination showed a spindle cell neoplasm considered to be a fibrosarcoma.

REVIEW OF THE LITERATURE

Testicular tumors in infants and children are rare. In the surgical literature beginning with Julien's collected series in 1925 and

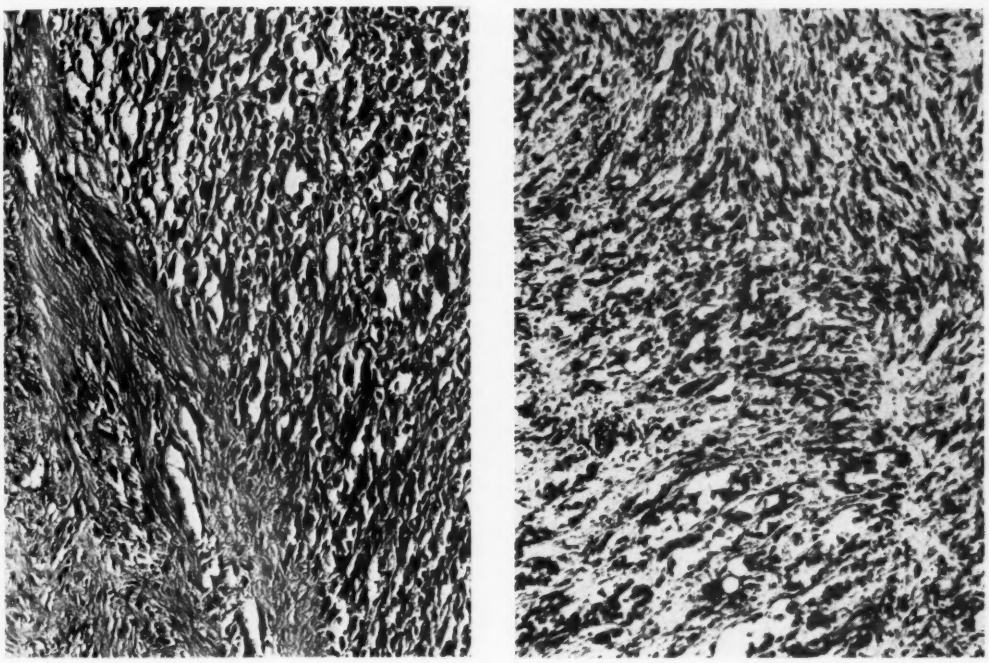

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FIG. 4. Sarcoma. a, Case 6. Undifferentiated sarcoma of the testis. No evidence of teratoid transformation (×130). b, Case 7. Undifferentiated sarcoma of the testis; probably a rhabdomyosarcoma (×110).

continuing through 1954, a total of 464 cases were reported (11). This figure includes the 137 cases reported by Julien and 171 cases collected by Guilleminet and Fourrier and reported in 1949. Except for those two large collected series, the vast majority of the literature devoted to the subject is limited to reports of single cases.

A critical examination of the reports of the 464 cases classified as testicular tumors in infants and children indicated that a large number do not have sufficient documentation to permit their reclassification on a histologic basis. In 185 of the cases, no pathologic data were given except statements that the tumors were testicular in origin. This group is composed essentially of cases included by authors in large series of adult testicular tumors or in papers devoted to the treatment of testicular tumors in both adult and pediatric age groups.

The remaining 279 cases of testicular tumors in infants and children were reported by the authors as specific types of gonadal tumors. However, the great majority were difficult to evaluate because the histologic description or photomicrographs were either lacking or unsatisfactory for definitive histologic classification. In addition, the clinical and follow-up data were in the majority of cases either not adequate or not presented at all.

Comparative incidence and malignancy. Despite the lack of detail encountered in our review of the literature, we were impressed by the finding that in the majority of case reports teratoma of the testes in infants and children was described as being a clinically benign tumor. Julien in 1925, and Rusche and Mostofi in more recent publications have commented on the benign behavior of teratoma of the testis in this age group.

The tumors of the testis reported by authors as embryonal carcinoma were the most difficult to evaluate, because of the conditions already stated. However, the tumors we accepted as embryonal carcinomas were clinically highly malignant neoplasms.

Seminomas and chorioepitheliomas appear to be extremely rare testicular tumors in the pediatric age group, if they occur at all. We found reports of 4 cases of "seminoma" of the testis and of 2 cases of "chorioepithelioma" of the testis occurring in infants and children. But the reports included neither detailed microscopic descriptions nor photomicrographs, and it was, therefore, impossible to accept them as proof of the existence of seminomas or chorioepitheliomas in this age group.

The present résumé does not offer a complete accounting of all morphologic variations of nongerminal testicular tumors. However, we did find interstitial cell tumors of the testis to be the commonest new growth in this group, as indicated by Mayers.

Noteworthy series. Although the information derived from review of the literature was limited in respect to the histopathology and clinical course of the patients whose cases were reported, a number of publications are worthy of special comment.

Julien, in the report of his findings from 137 cases of testicular tumors in infants and children, noted that more than half of the testicular tumors in these patients occurred during the first 5 years of life. Thirty-two tumors in his series were described as "teratomas" of the testis. He considered these tumors relatively benign, as metastasis was known to have developed in only 1 case. The remaining 105 lesions he classified as mixed tumors, with a comment on the difficulty of proper classification caused by their complex histopathologic pattern.

Mostofi reported the cases of 24 children with testicular tumors observed at the Armed Forces Institute of Pathology. Fifteen of these tumors were classified as embryonal carcinomas, 7 as teratomas, and 2 as of undetermined nature. He presented no follow-up data concerning the patients with the embryonal carcinomas. All of those with teratoma were reported as living and well, but the period of observation was not stated.

Dean studied testicular tumors of 8 patients in the pediatric age group. He gave the opinion that testicular tumors in these patients are clinically and histologically similar to their counterparts in adults.

Magner, Campbell, and Wiglesworth recently reported on 7 testicular tumors that they had studied in young children. They considered the tumors in this series to be a distinctive group, and used the term "adenocarcinoma with clear cells" to designate them. Three of his patients were living after 10 years, 7 years, and 6 years respectively. Two patients were alive and well without recurrence after 1 year, 4 months and 1 year, 5 months. Two patients had died as a result of their tumors, one 22 months and the other 8 months after the initial treatment.

Gross treated testicular tumors in 12 infants and children. No microscopic description accompanied his report. However, his follow-up study revealed that 1 patient with a teratoma was alive and well 4 years after simple orchiectomy. Seven patients were considered to have had embryonal carcinoma of the testis; 3 of these were living and well after 3 years or more and 1 patient was entirely well 1 year later; 3 patients died from the effects of their tumor within 1 year of their initial treatment. Of 2 children whose tumors were described as adenocarcinoma and carcinoma of the testis, the former was living and well for a period of 6 months while the latter succumbed 6 months after excision of the tumor. One patient who had had a seminoma of the testis at 11 years of age was living and well 3 years after simple orchiectomy.

Rusche collected reports on testicular tumors in 12 infants and children and described 8 teratomas, 3 embryonal carcinomas, and 1 dermoid. All patients with teratomas were living and well after 2 years

or more, as was 1 patient with the dermoid of the testis. Of the 3 patients with embryonal carcinoma, 1 was living and well 5 years after initial treatment, while the remaining 2 patients had succumed from the effects of their tumor within 1 year of operation.

COMMENT

Testicular tumors in infants and children are rare, as is shown by our finding of only 464 reports of such cases in the surgical literature. An additional 9 cases were found in the files of the Mayo Clinic and provided the basis of this report.

According to the review of the literature, teratomas of the testis in infants and children are clinically rather benign tumors. This finding is in contrast to the experience of Moore and Dixon with adult teratomas of the testis, in which they found a 5 year mortality rate of 29 per cent. In our 1 case, the teratoma of the testis showed a microscopic focus of malignancy. The patient, however, has survived 4½ years without evidence of recurrence. Thus, our study does not explain the apparent difference between the degree of malignancy of teratomas of the testis in adults and that of such tumors in children.

The 4 embryonal carcinomas of the testis in our series were highly malignant by both clinical and histologic standards, and no patient survived more than 2 years following initial symptoms. Such findings are comparable to those of reported series in adults.

The remaining 4 tumors in our series were sarcomatous in histologic appearance. In the 1 gross specimen suitable for anatomic study (Case 6), the tumor appeared to involve mainly skin and the testicular tunics. Centrally massive necrosis was found and no actual testicular tissue could be identified. In 2 other cases histologic involvement of smooth or striated muscle was noted on multiple block sections from the original tissue, but the gross specimens were no longer available for study. Moore and Dixon considered sarcomatous patterns in adult testicular tumors as malignant transformations of teratoid elements. However, in the multiple sections made from our sarcomatous tumors we were unable to find any evidence of teratoid structure. The fact that foci of muscle were present leads us to believe that these 4 tumors probably arose from the tunics of the testis or from the supportive muscle of the testis.

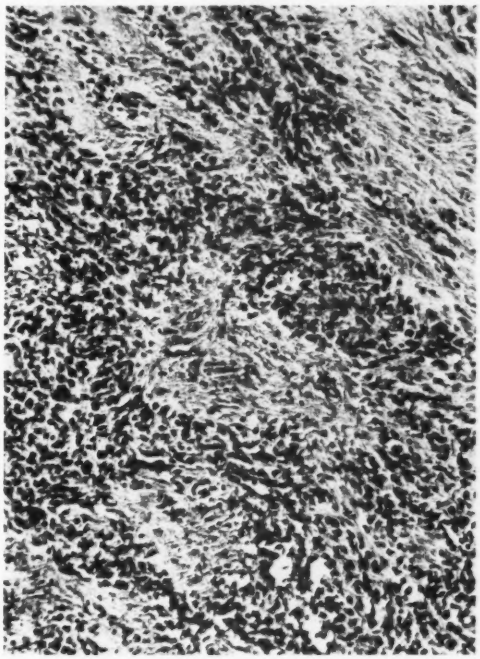

FIG. 5. Case 8. Irregular closely packed tumor cells resembling a sarcoma (×130).

We encountered no cases of seminoma or chorioepithelioma of the testis in our series, and the surgical literature indicates that these two types of neoplasm are extremely rare in the pediatric age group.

SUMMARY

Nine cases of testicular tumor in the pediatric age group have been described in clinical and histologic detail as seen at the Mayo Clinic. In addition, reports of 464 cases of testicular tumors in infants and children were discovered in a review of the surgical literature. Teratomas of the testis in

patients of pediatric age seem to be relatively benign tumors. Embryonal carcinomas are highly malignant, as are a group of tumors described in our own series as undifferentiated sarcomas. Seminomas and chorioepitheliomas in infants and children are pathologic rarities.

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PERCUTANEOUS TRANSFEMORAL SELECTIVE RENAL ARTERIOGRAPHY IN PATHOLOGIC CONDITIONS OF THE KIDNEY

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AFTER THE FIRST ATTEMPTS to visualize the branches of the abdominal aorta separately were made by Fariñas in 1941 and not further developed, attempts to accomplish the same purpose were later resumed by Radner and Brodén and associates in 1948, and by Bierman and associates in 1951. These investigators succeeded in visualizing some collateral vessels of the aorta by introducing a cardiac catheter, bent at its initial tip, into a previously prepared vessel.

To obviate the inconvenience of the cardiac catheter becoming exceedingly flexible at body temperature when in the blood stream and thus losing its initial curvature so that it could no longer be guided from without, Tillander (14, 15) replaced it by a special catheter, the end of which consisted of a series of small metal cylinders linked by ball and socket joints and which, by means of a strong magnetic field placed outside the patient, could be guided under radioscopic control and pushed up into the aortic branch that was to be visualized.

However, all these methods presented the disadvantage of requiring surgical measures which, though more or less important according to the artery chosen for insertion of the catheter, often involved some risk of postoperative thrombosis, necessity of ligating the vessel isolated, and wound infection.

Seldinger (4, 13) and Ödman (10, 11), independently of each other, devised very similar techniques, simpler than the preceding ones since they presented the great advantage of not requiring preparation of the vessel. These methods permit the introduction of the catheter percutaneously into the femoral artery by the aid of a special device, and passage of the catheter to the level of the aortic branch to be catheterized.

The present study was directed at investigating the arterial renal circulation in the presence of pathologic conditions.

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METHOD

We applied the method proposed by Ödman except that 1 to 2 hours before the angiographic examination was begun, all the patients were subjected to retropneumoperitoneum by introducing, via retrococcyx, 1 to 1.5 liters of oxygen.

The equipment consists of a "needle-cannula with a chuck," a comparatively flexible catheter which can be molded into the desired curved shape by warming, and a metal guide consisting of a steel spiral one end of which is less rigid than the rest. Moreover, the catheter presents two other important features: it is radiopaque and retains its shape at body temperature.

To perform selective arteriography of the renal artery, the femoral artery is punctured by means of the cannulated needle under local anesthesia (1 per cent novocain) immediately under the inguinal ring,[1] and, after removing the chuck, the flexible end of the metal guide is introduced through the

[1]The femoral artery chosen is, as a rule, the one on the same side as the renal artery to be visualized. In young, and especially tall, subjects as well as in some pathologic cases (e.g., thrombosis of a femoral artery), the catheter may be introduced through the contralateral femoral artery.

needle. After this has been withdrawn, the catheter is moved along the guide until it penetrates into the lumen of the vessel. When the catheter lies in the femoral artery, the metal guide is withdrawn, and the catheter is advanced under radioscopic control toward the heart of the patient until its tip—which is now in the circulatory tree—reaches the level of artery to be catheterized.

By suitable maneuvers, and always under radioscopic control, it is now possible to pass the tip of the catheter (previously fixed in the desired curved shape) into the artery.

At this moment, 10 to 15 cubic centimeters of contrast medium are injected, and, during the injection, a series of roentgenograms is performed. After completion of the radiographic examination, the catheter is withdrawn, when compression is exerted upon the point where the needle has perforated the femoral artery in order that an eventual hemorrhage may be checked.

The easy performance of selective angiography according to Ödman's method, the almost absolute absence of complications, and finally the possibility of introducing the catheter into the lumen of the vessel without surgical procedure are such signal advantages as to render this method decidedly superior to any other proposed hitherto.

In performing the first selective angiograms, no matter according to what method, Ödman's not excepted, examination of the vessel to be catheterized may involve serious difficulties, especially in subjects affected with arteriosclerosis. The tortuosity of the vessels compels the catheter to describe curves and countercurves which limit its maneuvering qualities and, in some cases, even prevent its progress. In this connection, it should be borne in mind that the progressive motion of the catheter is brought about by movements imparted to the part which remains outside, movements which are always comparatively imperative and restricted within narrow limits. But by experience a dexterity is acquired rendering catheterization of the vessel comparatively quicker and examination less traumatizing.

As to the eventual complications which may result from catheterization of an artery, it should be remembered that Bierman and associates, in a total of 24 selective arteriograms, observed only 2 cases of occlusion of the common carotid artery (they had isolated in order to introduce the catheter) with consequent contralateral hemiplegia, 1 case of infection of the surgical wound and aneurysm of the carotid attended by hemiplegia, and finally 1 case of thrombosis of the left brachial artery followed by gangrene of the homologous upper limb.

Morino and Tarquini, who recently applied the technique devised by Radner, were compelled to ligate the brachial artery into which they had introduced the catheter, after surgically isolating it, 3 times in 18 cases. As is well known, owing to the rich network of collateral vessels in the upper limbs, the occlusion of the brachial artery is almost always free from serious consequences. Nevertheless, should the stoppage be occasioned by thrombosis rather than by ligation—an event which may, though seldom, occur after catheterization of an artery—the consequences might be much more serious.

Ödman's technique presents the great advantage, in comparison with other methods, of not requiring preparation of the vessel, a fact which spares the arterial wall traumatization and lesions and thus eliminates one of the most important causes of thrombosis. On the other hand, this technique presents the disadvantage of using the femoral artery, which often lacks a sufficient collateral circulation, for introduction of the catheter.

Nevertheless, Morino and Tarquini's affirmation that "eventual lesions of the femoral artery due to preceding catheterizations may occasion even serious and irreparable anatomic and functional injuries" seems to be a too drastic one, especially if the data afforded by both the experience of the Swedish investigators and the present studies are taken into account.

Among all the patients subjected to percutaneous selective angiography, a single

FIG. 1.

FIG. 2.

FIG. 1. Case 1. Percutaneous selective angiography of the right renal artery. Scarce vascularization of the organ. The arteries are small in caliber and are rapidly decreasing; capillary network practically absent. Diagnosis: Hypoplastic kidney? Renal arteriosclerosis (secondary shrunken kidney)?
FIG. 2. Case 1. The left renal artery. Arteriographic finding, normal.

case of thrombosis of the femoral artery occurred during the maneuvers performed under radioscopy, the patient complaining of a sudden pain attended by a feeling of formication and cold in the limb homolateral to the point of introduction of the catheter. In this case it was necessary to intervene about 2 hours after angiographic examination, and the thrombus was removed from the femoral artery. Owing to this prompt action, practically no sequelae resulted. We later ascertained that this patient was affected with thrombophilic diathesis. Since this occurrence, before carrying out percutaneous selective angiography, we systematically perform laboratory tests with the view of establishing the blood coagulation power of the patients to be subjected to angiographic examination.

We wish to emphasize the use of retropneumoperitoneum. In practice this has helped us to identify the renal artery more quickly and to interpret the angiograms better. In fact, by isolating the kidney from the surrounding tissues and demarcating its contours, the retropneumoperitoneum renders it possible not only to locate this organ and consequently to make out the approximate point of origin of the renal artery but also to visualize the course of the vessels, especially in their terminal parts.

We have examined by this method 35 patients affected with various renal diseases, but only those cases which disclosed a decidedly pathologic picture are reported here.

CASE REPORTS

CASE 1. A. I., a 58 year old man, complained of a feeling of weight in the right side of a few years' duration and of moderate intermittent hematuria for a few months. The urogram showed "functional silence" of the kidney on this side; normal findings on the left side. The retropneumoperitoneum was inconclusive regarding the condition of the right kidney because the oxygen did not reascend into the right renal artery in the quantity required.

Percutaneous selective angiography of the right renal artery was performed by introducing 13 cubic centimeters of 50 per cent joduron after catheterization of the right femoral artery. A notable scarcity of arterial vessels with a rapid reduction of caliber and

FIG. 3.

FIG. 4.

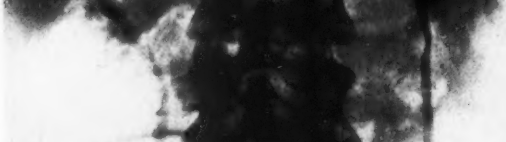

FIG. 5.

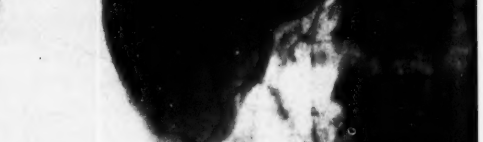

FIG. 6.

FIG. 3. Case 2. Urogram showing a defect of filling, involving the inferior calyces and the lower part of the renal pelvis, as if an extrinsic mass were compressing these formations.

FIG. 4. Case 2. Percutaneous selective angiography of the right renal artery. The lower branch of the renal artery presents an abrupt angulation and its interlobar tract assumes a rectilinear direction, losing the usual sinuosity of its course. The minor vessels branching off from this branch have unequal calibers and circumscribe a zone of parenchyma scarcely supplied and less opaque with respect to the remaining renal tissue. The surrenal artery is visible at its direct departure from the main renal branch. Diagnosis: (Necrosed?) malignant tumor of the caudal pole of the right kidney.

FIG. 5. Cut surface of specimen from Case 2. The neoplastic tissue, partly necrosed and exceedingly friable, occupies the lower part of the renal pelvis.

FIG. 6. Same as Figure 5, after removal of the neoplastic mass.

nearly complete exhaustion of the circulation at the level of the cortex (Fig. 1) was observed. The nephrographic effect was practically absent, and the kidney appeared undersized.

At the same time a percutaneous selective angiogram of the left renal artery was taken (Fig. 2). A normal arterial circulation was observed with big vessels and numerous ramifications.

The diagnosis which was made in this instance was questionable hypoplasia of the right kidney or arteriosclerosis of the right kidney (secondary shrunken kidney).

CASE 2. A. P., a 49 year old man, complained of pain of rather long standing in the right flank radiating to the thigh, hematuria, pollakiuria, asthenia, and emaciation.

The urogram (Fig. 3) revealed a defect of filling involving the group of the inferior calyces and the pelvis of the right kidney, and on the left side, normal findings.

Percutaneous selective angiography of the right renal artery (Fig. 4) was carried out by introduction of 15 cubic centimeters of 50 per cent joduron after catheterization of the homolateral femoral artery. The lower branch of the right renal artery presented a sharp angulation while its interlobar tract assumed a rectilinear direction, losing the usual sinuosity of its course. The minor vessels branching off of it presented different, abnormally nondecreasing calibers and seemed to circumscribe an area strikingly poor in vessels, well evidenced, also in the nephrographic phase, by a decided diminution of opacity. The surrenal artery was also visible at its direct departure from the main renal branch. The diagnosis was malignant tumor, partly necrosed, of the inferior pole of the kidney.

On surgical intervention the lower pole of the right kidney appeared slightly enlarged; palpation revealed a mass, the size of a nut, of soft elastic consistence, occupying the renal pelvis. Nephrectomy was performed. The section of the kidney removed showed a neoplastic mass almost completely occupying the inferior calyces and the lower part of the renal pelvis (Fig. 5) though respecting its walls. This mass, at its departure from the lower pole of the kidney, consisted of partly necrosed tissue, so friable as to be almost totally removed during the delicate lavage of the anatomic specimen (Fig. 6).

Histologic examination showed "tubular adenocarcinoma." Radiography, performed after introduction of a radiopaque substance into the main artery of the kidney removed (Fig. 7) confirmed the observations made by means of the selective angiography.

CASE 3. S. M., a 69 year old man, had suffered from pollakiuria and hematuria of 1 year's duration and complained of a feeling of weight in the right flank.

Urography (Fig. 8) showed an enlargement of the whole right kidney. The middle and inferior calyces, on this side, appeared divaricate and compressed, as if a mass of regular spherical contours, such as may be observed in cystic forms, was insinuating between them. The absence of an intimate involvement of the pyelitic walls as well as their regular and gradual deformation might suggest a prima facie diagnosis of a big renal cyst.

Percutaneous selective angiography of the right renal artery (Fig. 9), carried out after introduction of 15 cubic centimeters of 50 per cent joduron and by catheterization of the left femoral artery, showed that all the branches of the renal artery were dislocated toward the cephalic region of the organ. The vessels of the middle and lower part of the kidney followed a tortuous course initially and terminated in a net-

FIG. 7. Case 2. Injection of barium suspension (mélange) into the right renal artery. No visualization of the arterial, medullar and cortical, branches of the inferior polar region.

work of pathologic character, in which no sign of vasal architecture was any longer recognizable, and eventually resulted in vast amorphous spots of the blood lake type (Fig. 10), typical of malignant neoformations (such as hypernephroma). The diagnosis was malignant tumor of the lower pole of the right kidney.

On surgical intervention the inferior pole of the right kidney appeared notably enlarged (Fig. 11), yellowish, and presenting a knotty surface; nephrectomy was therefore performed.

Section of the anatomic specimen revealed (Fig. 12) that the lower half of the kidney consisted of newly formed tissue, yellow in color and lardaceous in appearance, presenting irregular contours. Histologic examination confirmed the presence of a clear-cell carcinoma (hypernephroma). Radiography of the anatomic specimen performed after introduction of a radiopaque substance into the main artery of the kidney removed (Fig. 13) corroborated the observations made by means of the selective angiography of the renal artery.

CASE 4. L. F., a 27 year old woman, complained of a feeling of weight and moderate pains in the left flank of several years' duration. No hematuria nor any other urinary symptoms were present. Objective examination revealed a mass the size of a fetal head,

FIG. 8. Case 3. Urogram. The middle and inferior calyces of the right kidney appear divaricate, deformed, and compressed by an intrinsic mass with prevailingly extrapelvic development.

oblong, with a smooth surface, of hard elastic consistence, mobile both passively and during the respiratory movements, indolent. The lower margin of said mass reached 2 transverse fingers below the iliac wing.

Urography showed "functional silence" on the left side (Fig. 14). From this side it was impossible to perform an ascending pyelographic examination inasmuch as, on cystoscopy, the left urethral outlet into the bladder was not found.

Percutaneous selective angiography of the left renal artery (Fig. 15) was carried out after catheterization of the right femoral artery. Ten cubic centimeters of joduron were introduced. The origin of the renal artery lay in its usual position. The main vessel was thin and did not differentiate, as to its caliber, from the successive branches. The interlobar and interlobular vessels were thin, their caliber uniform, scarcely dichotomized. The renal parenchyma was represented by small islets of tissue in which the arteries were distributed in tufts. The nephrographic image was limited to these small areas which appeared to be separated by large zones, roundish and transparent.

Since the patient refused surgery, it is impossible to furnish an anatomicopathologic diagnosis. Nevertheless, on the basis of the clinical and arteriographic findings, our diagnosis was a "giant hydronephrosis," a hypothesis suggested by the following elements: abnormal enlargement of the renal hilum, elongation of the main arterial vessels whose uniformity of caliber was characteristic of a slow, gradual development of the organ, absence of the functional renal parenchyma, obviously destroyed because of some compressive mechanism connected—in our opinion—with the dilatation of the pyelitic cavities, and finally unilaterality of the condition (the percutaneous selective angiography of the right renal artery, Fig. 16, evidenced, in fact, a normal kidney).

In this case, a diagnosis of "polycystic kidney" might have been put forward as well; but it seemed to us that such a diagnosis was untenable and should be discarded since the morbid process involved not only the parenchyma but also the renal pelvis, as the abnormal enlargement of the hilum revealed.

CASE 5. A. S., a 60 year old man, about a month before in perfectly good health, suddenly remarked hematuria of the terminal type, pollakiuria, especially in protracted orthostatic position, and vesical tenesmus. This first event was followed by a second 10 days before admission to our clinical hospital.

Urography showed "functional silence" on the left side.

On cystoscopic examination the presence of a tumefaction of the shape and size of a pigeon's egg, covered with hyperemic mucosa, was observed in correspondence with the urinary meatus. The tumefaction was sessile and presented rare contractile movements. The urethral meatus, so restricted as not to permit the passage of the catheter, was visible on its summit. Ascending pyelography was, therefore, impossible.

Percutaneous selective angiography of the left renal artery was carried out after catheterization of the right femoral artery (since the left one presented signs of partial thrombosis) and by introduction of 10 cubic centimeters of 50 per cent joduron. The upper pole of the left kidney was entirely depopulated. No impression was observed on the renal artery, and retropneumoperitoneum showed that the upper pole of the kidney was not enlarged and presented regular contours (Fig. 17).

The most tenable hypothesis put forward after percutaneous selective angiography was the one pointing to a "defect of vascularization of the upper pole of the left kidney." The regularity of the kidney contours, so well evidenced by the retropneumoperitoneum, as well as the absence of anomalous vessels and a pathologic capillary circulation (blood lakes) rendered the

FIG. 9.

FIG. 10.

FIG. 11.

FIG. 12.

FIG. 9. Case. 3. Percutaneous selective angiography of the right renal artery (arterial phase). The branches of the renal artery are dislocated toward the cephalic region of the organ and their ramifications appear immediately tortuous and slightly dilated owing to obvious difficulty of discharge. The arteries of the lower half of the kidney are not visible.

FIG. 10. Angiography of the right renal artery (capillary phase). In the lower part of the kidney the vascular net is pathologic, characterized by vast spots of the "blood lake" type. Diagnosis: Malignant tumor (of the hypernephroma type) of the caudal pole of the right kidney.

FIG. 11. Gross specimen from Case 3.

FIG. 12. Cut surface of specimen from Case 3.

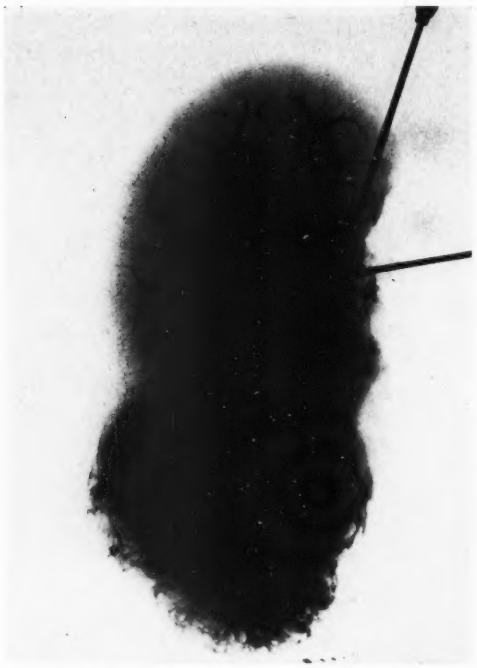

FIG. 13. Case 3. Injection of barium suspension into the right renal artery. Same result as with percutaneous selective angiography.

presence of a pathologic process involving the parenchyma exceedingly doubtful.

On surgical intervention the existence of an upper polar vessel, directly originating from the aorta, was ascertained. The clinical symptomatology was due to a ureterocele (whose presence had been suggested by the cystoscopic finding) which was subsequently treated endoscopically and by electroresection.

DISCUSSION

On the basis of our experience we believe that renal percutaneous selective arteriography constitutes a most practical method for solving problems which, otherwise, could not be easily cleared up.

The chief interest of this study resides in the possibility of visualizing the structural abnormalities of the kidney through the architectonic representation of the arterial vessels. The seriographic study on injection of the contrast medium permits us to observe the gradual filling of the vessels and their distribution, two important factors in a systematic investigation of the manner in which arteries and capillaries ramify.

Apart from the often glaring variations of the main arterial branches, careful attention should be devoted to the study of arciform arteries, particularly of the interlobar arteries, since these vessels are of the utmost importance from a diagnostic viewpoint. Of less importance is the stage of total opacification of the organ, which is reached only too late, for in this phase it is impossible to bring to view changes of vessel tone conducive to a more correct interpretation of the radiologic pictures.

On the first radiograms of normal individuals the chief vessels of the kidney maintain, in spite of inevitable superpositions, a distinct individuality uniformly distributing their sinuous branches close to the cortex where, after some minor subdivisions, they suddenly terminate and end in the capillary bed. This course varies according to age: in elderly subjects a greater tortuosity of the chief branches and a lesser abundance of secondary ramifications with reduced opacification of the capillaries is observed. These anatomic radiographic acquirements are important for the interpretation of the pathologic pictures, especially with respect to the differential diagnosis of each separate form of disease.

The radiographic pictures which may be obtained under pathologic conditions may be reduced to three fundamental types respectively characterized by: (a) absence of the vascular network in a particular sector; (b) deviation or amputation of one or more vessels; (c) appearance of a pathologic vasal network.

Taking into account the fact that these images may also be variously represented in one and the same picture, the possibility for a differential diagnosis, especially in the delicate province of benign and malignant tumors, can only emerge from a thorough study of the course of the arterial branches. It so happens, for example, that a sharp stop or crowding of the vessels as against a compact and rigid obstacle evidences the

FIG. 14.

FIG. 16.

FIG. 15.

FIG. 14. Case 4. Urogram with compression on the ureters. "Functional silence" on the left side. On the right side, normal secretory activity with precocious, intense appearance of opaque urine showing a moderate but uniform dilatation of the pyelic cavities.

FIG. 15. Case 4. Percutaneous selective angiography of the left renal artery. Abnormal elongation of the main vessels with poverty of peripheral subdivisions, limited to capillary tufts, and absence of supplied parenchyma. Diagnosis: Giant hydronephrosis of the left kidney.

FIG. 16. Case 4. Percutaneous selective angiography of the right renal artery. Regular distribution of the vessels as in young subjects.

presence either of a cyst or a hydronephrotic cavity, whereas the finding of small deviated vessels or vessels of unequal calibers attests to the presence of a neoplastic mass.

Some surprise may be excited by the anomalous vessels originating directly from the aorta (see Case 5), inasmuch as they supply segments of organs which, on radiographic examination, appear completely depopulated, with a misleading appearance of pathologic encumbrance. The deviation from Ödman's method which we suggested, i.e., the systematic use of retropneumoperitoneum, seems to be particularly useful in these studies, since it affords a better defined image of the size and contours of the kidney.

As to the anomalous renal vessels directly originating from the aorta, aortography, by demonstrating all the collateral vessels at the same time, affords surer and more consistent results. However, such a method may be applied only in a limited number of cases considering not only the risk this tech-

FIG. 17. Case 5. Percutaneous selective angiography of the left renal artery. No opacification of the upper pole of the kidney owing to autonomous supply from polar vessel directly from the aorta. Retropneumoperitoneum permits observation of the regular morphology of the organ, and particularly of the upper pole, which excludes any possibility of intrinsic neoformative lesions. Diagnosis: Defect of vascularization owing to anomalous polar vessel directly departing from the aorta.

nique involves but also the incidents which are liable to occur later on, especially with respect to renal function. In fact, Idbohrn and Berg demonstrated, on the basis of experiments carried out in rabbits, that the injection of 50 per cent umbradil provokes alterations, though of transitory nature, of the renal parenchyma attended by modifications of the permeability of the glomeruli and notable albuminuria (17.5 per cent or more) whether the contrast medium is introduced into the carotid, the renal artery, or directly into the aorta. In the course of aortographic examinations, Alwall and his associates observed 8 cases of renal suffering followed by 2 deaths. Miller and his associates, in a series of 250 aortographies, had an incidence of renal damage of 3 per cent.

Clinical and experimental results demonstrated that the renal damage after aortography depends on both the high pressure under which the contrast medium is injected and its toxicity, consequently in proportion to the amount employed. Now, whoever is conversant with aortography knows that to obtain satisfactory results high pressure on introduction as well as high concentration of the contrast medium cannot be dispensed with. It follows that renal selective angiography is far less dangerous than aortography, and insures decidedly superior results. The advantage of selective angiography with respect to aortography resides in the fact that, by the former, it is possible to study the pathologic kidney alone and to expose it to comparatively little trauma, since a small amount of contrast medium and a low pressure are required. This method enabled us to make some otherwise rather puzzling diagnoses, and furthermore supplied such exact information concerning the site and extent of the pathologic lesions as to indicate less extensive surgical intervention.

SUMMARY

In 35 patients affected with surgical diseases of the kidney, percutaneous transfemoral selective renal arteriography was carried out according to Ödman's method. All the patients were subjected, 1 to 2 hours before percutaneous selective angiography, to retropneumoperitoneum, a procedure which proved very useful both for easier identification of the renal artery and for obtaining a greater contrast of the visualized vessels.

The most interesting cases are reported and discussed.

Percutaneous transfemoral selective renal arteriography proved a comparatively simple examination, almost free from complications, of great practical value, especially in those cases in which neither clinical nor urographic examination had indicated a certain diagnosis.

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NONOSTEOGENIC FIBROMA OF BONE

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NONOSTEOGENIC FIBROMA is a benign defect in the metaphyseal region of the long bones, displaying rather characteristic histologic and radiologic features, and occurring predominantly in young people. It is controversial whether it is a neoplasm, a developmental defect, a reaction to injury, or a residue of inflammation.

In 1921, Phemister concluded that these lesions are inflammatory and introduced the term chronic "fibrous" osteomyelitis. Schroeder and others, described similar defects under the name of "xanthic giant cell tumors," calling attention to the foam cells and giant cells commonly present in the lesion. Burman and Sinberg, along with Jaffe, looked upon the disease as a solitary xanthoma, or a form of "lipoid granulomatosis;" and later, in 1942, Jaffe and Lichtenstein introduced the term "non-osteogenic fibroma," while at the same time Coley and Miller referred to them as "atypical giant cell tumors." Hatcher expressed his opinion that these lesions are not true neoplasms; he therefore proposed the more noncommittal term "metaphyseal fibrous defect." Schlumberger and others considered the disease a form of fibrous dysplasia. It is due to this disparity of opinion that we have been prompted to record our observations on 20 patients with this lesion. Recognition of this rather common entity by surgeons and pathologists will be facilitated by the acceptance and use of uniform diagnostic terminology.

INCIDENCE: SEX PREDOMINANCE AND AGE DISTRIBUTION

The frequency of this condition is not accurately known because of two factors: (a) disagreement exists among observers with regard to diagnostic nomenclature for this lesion; (b) and many are probably asymptomatic and are never discovered. It is more common than generally believed. Sontag and Pyle in periodic serial studies of 200 otherwise healthy children, found cortical defects consistent with this lesion in 54 per cent of boys and 22 per cent of girls at one age or another. Similarly, Caffey concluded that between 7 and 20 per cent of all knee joints examined radiographically between the ages of 2 and 12 years will exhibit such defects. Though in private practice these lesions are frequently encountered, it is our impression that clinically they are not seen quite as often as these figures suggest. The sex incidence is variable and is difficult to assess properly. Clinically it is encountered more frequently in males than in females, but it has been suggested that the increased frequency of trauma in boys may account for a greater number of roentgenograms being taken, thus uncovering more asymptomatic lesions. On the other hand, Sontag and Pyle found a 5 to 2 male predominance in their random study. It is identified most frequently in individuals between 8 and 20 years of age. It has not been reported in boys younger than 2 years and in girls younger than 4, and it is rarely observed in individuals older than 20.

ROENTGENOGRAPHIC APPEARANCE

Roentgenologically, it represents one of the most distinctive lesions of the skeleton with respect to size, shape, location, and over-all appearance. It is consistently metaphyseal and eccentric in location. It may consist of a very small, oval defect in the periphery of the cortex (Fig. 1a), or it may extend into the medullary cavity, occupying a considerable width of the bone (Fig. 1b); or it may involve the entire thickness of a

a b

FIG. 1.

FIG. 1. Roentgenograms of 12 year old patient, who complained of mild pain in the right knee. a, The small eccentrically situated cortical lesion can be seen clearly (arrow) in the distal metaphysis of the femur on the lateral side. Note the gently scalloped border of bone, slightly increased in density which appears to separate the lesion from the remainder of the femur. Biopsy showed typical histologic findings of a nonossifying fibroma. b, X-ray film of 12 year old patient, whose first symptom of the lesion was a fracture following minimal trauma. After the healing of fracture, the entire area was resected and bone grafted. The lesion involves a major portion of the entire width of the bone. The scalloped border is prominent, and, although it appears to have septate loculations, this is deceiving; the septa do not traverse the center of the lesion, but rather represent ridges in the bony wall. The entire histologic section is shown in Figure 11a.

FIG. 2.

FIG. 2. Roentgenogram of a 12 year old patient whose first symptom was a fracture through the lesion incurred when she twisted her ankle. The lesion is located in the metaphysis of the fibula; it involves the entire width of the bone, and exhibits a scalloped, sharply circumscribed, irregularly loculated shape. This lesion was resected and a sliding bone graft was performed.

bone in such thin bones as the fibula, ulna, and radius (Fig. 2). It is radiolucent, oval in shape, and usually longer than it is wide. Only occasionally does one exceed 5.0 centimeters in length and rarely more than 1 lesion may exist in the same bone (Fig. 3).

The periphery is sharply demarcated from the surrounding bone in all cases. The larger lesions often exhibit irregular, smooth loculations, separated from the marrow cavity by a thin "scalloped" zone of sclerotic bone. The loculations are more apparent than real, being represented by ridges of increased density in the wall of the lesion (Fig. 4b). Occasionally, peripheral lesions may exist, which extend outward from, and usually communicate with, the main lesion(Fig. 5b). Rarely, there may be no significant peripheral zone of increased density, and the lesion may appear merely as an oval, punched-out lesion, eccentrically situated in the metaphyseal cortex of a long bone. The roentgenographic diagnosis would be uncertain with such findings as these (Fig. 6a and b).

PATHOLOGY

When examined en bloc, the periphery of the defect is usually well circumscribed by a thin layer of compact bone of variable thickness (Fig. 7a and b). The borders are often scalloped. The contents of the lesion presents a honeycomb mosaic of yellow, grey, and different shades of brown. In a general way, these different areas represent the tissue types found in the lesion; thus, the yellow areas represent xanthic or cholesterol histiocytosis or even fatty marrow; the gray zones are composed of fibrous tissue; the brown tissue contains hemorrhage, pigment, fibrous tissue, and giant cells. Mixtures throughout the lesion are usual.

a b

FIG. 3.

FIG. 3. Roentgenograms of patient who sustained a traumatic fracture of the middle shaft of the tibia. There were no previous symptoms. The presence of 2 typical nonossifying fibromas was noted. Both these lesions were curetted and packed with bone chips.

a b

FIG. 4.

FIG. 4. a and b, Roentgenograms of both legs of an 18 year old colored male, who complained of a lump over the medial upper aspect of the right leg. An osteochondroma of the proximal end of the right tibia and an eccentrically situated cortical lesion in the proximal metaphysis of the left tibia were demonstrated. Both lesions were resected. The histologic section of the surgical specimen is seen in Figure 7a.

Microscopically, the principal component is fibrous tissue intermingled with a variable number of giant cells (Figs. 7b and 8b). The fibrous tissue is uniform and benign, containing whorls and bundles of spindle cells. The giant cells are consistent in size, having a pale blue cytoplasm and containing usually 3 to 10 nuclei in each cell (Figs. 8c and 9). For this reason it is not uncommon for these lesions to be mistakenly reported as giant cell tumors, particularly when the patient's age, the locations of the lesion, and the radiographic picture are not known by the pathologist. Histologically, however, the resemblance of this lesion to true giant cell tumor of bone is only superficial; and with careful study, one should not be confused with the other.

Other microscopic features include hemorrhage, hemosiderin, cholesterol "slits," and focal collections of foam (xanthoma) cells (Fig. 10). Xanthoma cells are present in many, but probably not all. One of the important distinguishing features is the absence of any bone formation within the lesion per se; this obtains in all cases not complicated by fracture. Since most of these lesions are subjected to curettement rather than block excision, thorough tissue study may not be possible in all cases, and certain of the elements previously described may not be encountered.

One or another of these histologic features often predominates in any section or in any lesion. Consequently, one lesion may consist almost exclusively of spindle cells and giant cells; another may exhibit abundant collections of foam cells interspersed throughout a spindle cell stroma; or another may have a random sampling of all elements. To a certain extent, this is governed by the source of the specimen; also, it is conceivable that these differences may represent various stages in the development of the lesion. However, the total histologic picture throughout the evolution of the defect is not well known; and it is not clear which cytologic features predominate in different stages of progression and healing. A histologic study of a circumscribed, sclerotic, presumably healed defect in an adult is not known to us and has apparently not been reported.

a b

FIG. 5.

FIG. 5. a and b, Roentgenograms of patient who sustained a fracture of the medial malleolus of the right leg in July 1953. The lesion in the left distal tibial metaphysis was discovered incidentally when comparative roentgenograms of the opposite limb were obtained. The patient had no symptoms referable to this lesion. The surgeon elected to observe this patient, and 3 years later (March 1956) questionable enlargement of the lesion was noted (b). The apparent enlargement is probably due to the difference in view. The patient still has no symptoms and operative treatment is not being contemplated at this time.

a b

FIG. 6.

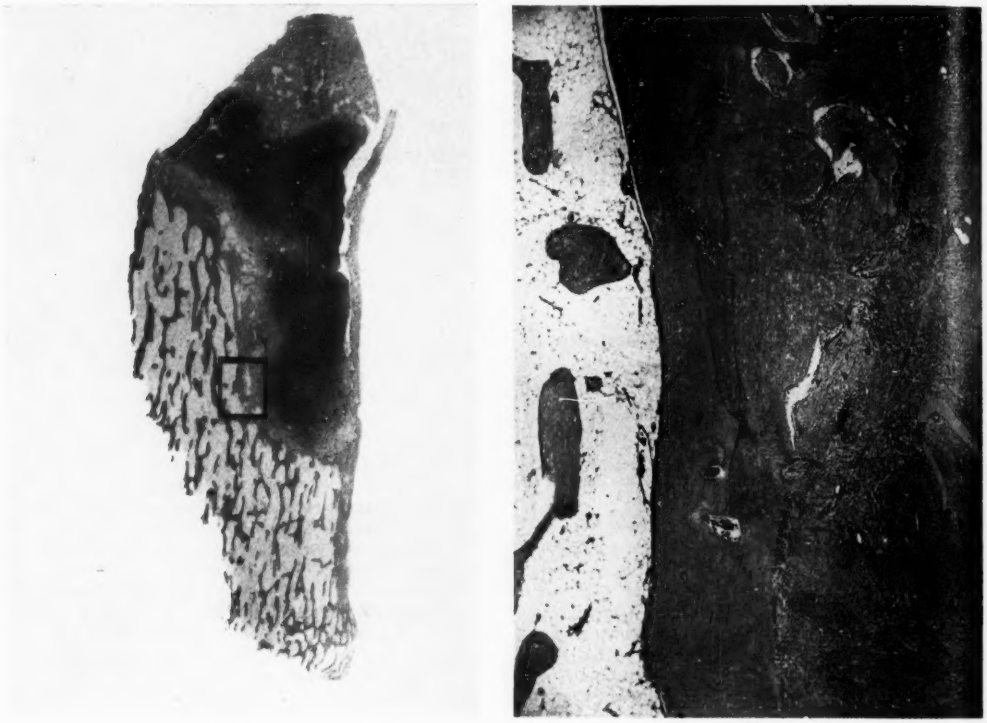
FIG. 6. Roentgenograms of a 12 year old patient who sustained a slight twisting injury and suffered a fracture through the femur at the level of the lesion demonstrated. a, The oblique view reveals what appears to be a centrally situated punched-out lesion in the metaphysis of the distal femur. This particular lesion does not have a scalloped periphery, and the bone immediately adjacent does not possess the usual increased density. b, The lesion occupies an eccentric position, characteristic of that found in nonossifying fibromas. This illustrates the importance of multiple views for diagnosis. The lesion was curetted and bone-grafted, after healing of the fracture.

In those cases which have been subject to recent fracture, additional microscopic features may be added which are manifestations of the healing callus. It is not uncommon then to have areas of fibrous bony callus (Fig. 11a and b). In some instances these may be mistakenly interpreted as integral parts of the lesion; and they can thus be confused, on superficial examination, with such conditions as fibrous dysplasia. It is therefore important that the tissue under study actually contain a bona fide portion of the lesion rather than the healing reaction of earlier trauma, and it is helpful also to know whether or not fracture through the lesion has occurred.

PATHOGENESIS

Though the pathogenesis of this condition is not wholly understood, some behavior characteristics are well-known. Using serial x-ray studies, Hatcher followed these lesions through various stages of development. It was found in the early stages, that there is a limited area of reduced density in the metaphysis, either central or peripheral, which lies very close to the epiphyseal disc. With bone growth, the defect moves further away from the epiphyseal plate; and during the process of tubulation, the defect eventually occupies part of the cortex of the bone, becoming predominately a peripheral, cortical lesion.

Accepting this method of development, several ultimate manifestations may be postulated; the defect may remain small, in the periphery of the cortex, giving rise to little or no symptoms and persisting as a typical "cortical defect"; it may increase in size, extending into the medullary cavity, but remaining principally confined to the cortex; or it may involve a significant portion of



a b

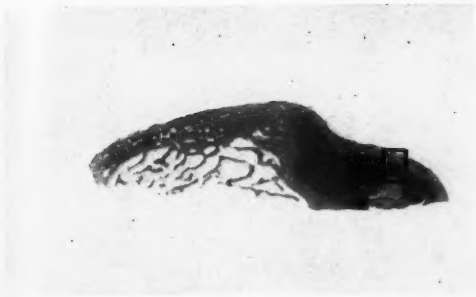
FIG. 7. a, Low power view of an en bloc section of the specimen demonstrated in Figure 4b. Note the dense, uniform appearance of the lesion which is sharply demarcated from the surrounding bone. ×2.7. b, High power view of the rectangle marked in (a). The bone at the periphery of the lesion, though increased in compactness, is normal in its over-all pattern. The sharp demarcation between the lesion and the normal marrow is well demonstrated. Note the osteoblasts on the surface of many of the trabeculae on the lesion side of the bony wall. Osteoclasts can also be seen. Fibrous tissue and spindle cells typical of this lesion are conspicuous. ×19.

the width of a bone such as the tibia or femur, or the entire width of the fibula, radius, or ulna. In these latter cases a predisposition to fracture may result. If the defect does not progress to this magnitude, it is likely that it will "heal," either by total replacement through growth and tubulation; or by simple ossification, resulting in a circumscribed zone of increased density in the metaphysis of a long bone.

From a clinicopathologic standpoint, it is well established that these defects do not recur following adequate curettement, or excision; and one has never been reported to be or have become malignant. Whereas solitary lesions are most common, multiple lesions have been reported in the same patient; and they have been seen to appear, disappear, and then reappear some years later in a similar location in the same bone. Not infrequently, as Hatcher noted, cases of nonosteogenic fibroma are associated with defects in enchondral growth, such as cartilaginous exostoses, and osteochondritis (Fig. 4a and b). This may be purely coincidental, or there may be an etiologic interrelationship between the two, thereby adding credence to the developmental theory of origin of nonosteogenic fibroma.

CLINICAL SYMPTOMS

The clinical manifestations of this condition are not remarkable. Usually attention is drawn to the lesion following some form



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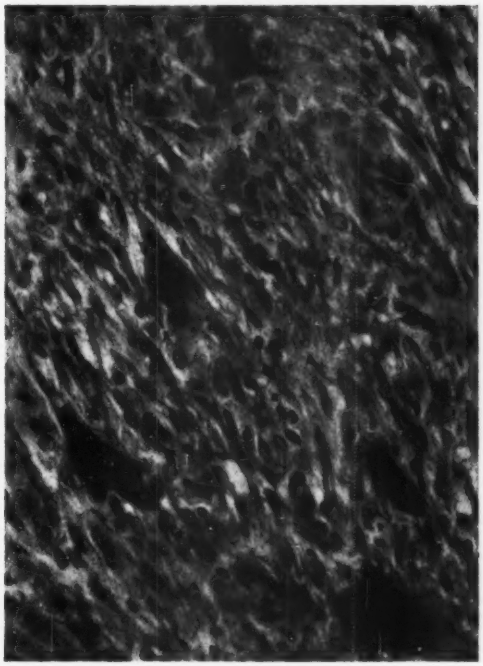


c

FIG. 8. a, Low power view of a section taken from a specimen removed en bloc. The densely staining, uniform appearance of the lesion is apparent. It is sharply demarcated from the rest of the bone by a heavy layer of compact bone. The marrow spaces of the uninvolved portion appear normal, and the trabeculae appear normal grossly. ×1.8. b, Photomicrograph of the rectangle outlined in (a). The tip end of the cortex, seen at the upper right-hand corner, blends inperceptibly with the fibrous portion of the lesion. The fibrocellular nature of the lesion is apparent throughout the section, and a generous number of multinucleated giant cells can be seen scattered evenly throughout the lesion. ×95. c, High power view of the giant cells and spindle cell stroma exhibited in (b). The cells of the stroma are oval and spindle-shaped. They are benign in appearance and uniform in size. There are no mitotic figures. The giant cells exhibit from five to fifteen nuclei per cell and are relatively clearly separated from the surrounding stroma. ×197.

of trauma, and the first symptom is a fracture in a sizable number of cases. Lesions which occur at the site of a muscle or tendinous attachment may be symptomatic, but when symptoms are present, they are usually mild. The majority of these defects are discovered incidentally, the patient having no symptoms directly referable to the fibrous lesion.

OBSERVATIONS

We have studied a total of 20 cases of this lesion in the Registry of Bone and Joint Pathology at Northwestern University Medical School. In 18 instances there was tissue available for study. In 2, the lesion was not operated upon, the diagnosis having been made by the characteristic radiographic picture. In 3 cases the defect was excised en

FIG. 9.

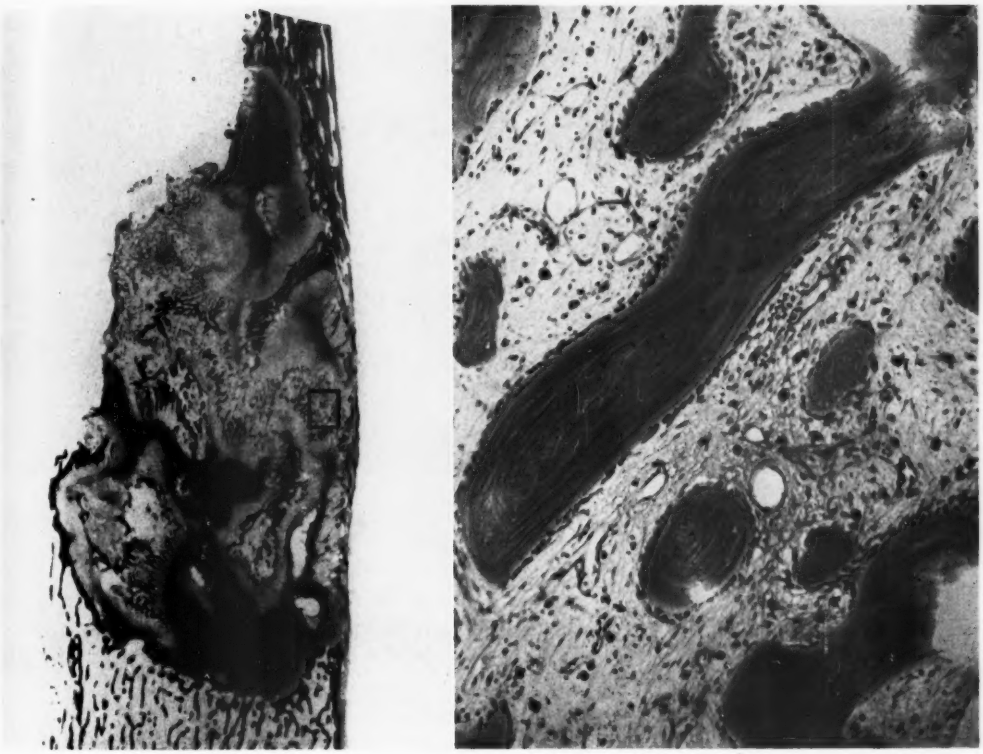
FIG. 9. High power view of the junctional tissue between the peripheral, sclerotic bone, and the lesion per se. Note the moderate fibrosis of the marrow in the adjacent bone trabeculae and the moderate amount of osteoclasis on the adjacent bone. It appears that the lesion exerts a mildly osteoclastic effect on the bone at its periphery, while at the same time the osteoblasts lay down new bone, thereby producing the thin sclerotic layer of bone which separates the lesion from the remainder of the bone. ×91.

FIG. 10.

FIG. 10. Photomicrograph of a section of a nonossifying fibroma in which the fibrocellular element is interspersed with numerous focal collections of foam cells, hemorrhage, and cholesterol deposits. In all 3 specimens which were removed en bloc, areas such as this could be found. ×91.

bloc (Figs. 7a, 8a, and 11a), thereby providing opportunity for detailed study of the entire lesion in situ, as illustrated and described earlier. The age at diagnosis, skeletal location, sex distribution, presenting symptoms, presence of other coexisting lesions, preoperative diagnosis, and follow-up results are all tabulated in Table I. These data are herewith briefly analyzed.

Thus, the lesions were encountered in patients between the ages of 10 and 21, the average age being 14 years. Five were located in the distal femur, 6 in the proximal tibia, 8 in the distal tibia, and 1 in the fibula. There were 7 females and 13 males, a ratio of nearly 1 to 2, which, owing to the small number of cases, is obviously *not* statistically significant. Coexisting skeletal lesions of another sort were found in 3 cases. It is significant that in 7 of 20 cases (35 per cent) the initial symptom which drew attention to the existence of the defect was a fracture through the lesion (Fig. 13). In some cases, the trauma which precipitated the fracture was very minimal. In others, symptoms were mild, or absent. An incorrect preoperative diagnosis was made in 12 of 20 (60 per cent). To date there have been no recurrences after operation, and in 2 patients not operated upon, one lesion has remained stationary in size, with a followup of 1 year, and the other has increased, approximately commensurate with an increment in skeletal growth (Fig. 5a and b).



a b

FIG. 11. a, Low power view of a section from an en bloc excision of the lesion seen in Figure 1b. The central portion of the lesion has been interrupted by a fracture which can be seen passing obliquely through the lesion proper. The dark staining areas represent the remnants of the lesion, and under high power view these areas show the typical features previously illustrated. Note again the sharp demarcation of the lesion from the remainder of the bone. ×2.2. b, High power view of the rectangular area illustrated in (a). This demonstrates the type of bone formation which occurs as a healing reaction in these lesions following fracture into or through them. Sections such as this lead some individuals to make a diagnosis of fibrous dysplasia. ×105.

DISCUSSION

It is our opinion that the small, eccentrically situated metaphyseal defect and the larger lesion most often diagnosed as nonosteogenic fibroma are variations of the same condition. Although the smaller, simple cortical defect is more often found in the younger (6 to 12) age group; and the larger, more extensive lesion is observed in patients between 10 and 20 years old, from the common sense standpoint there is no logical basis for separating the two. Radiographically they are similar, and histologically they are identical. Except for those which attain large size, in which case fracture might occur, they are clinically indistinguishable. They exhibit the same lack of symptoms, and they have the same sex distribution and skeletal location. The only real difference is that of size; and such individual differences are the rule in any lesion, benign or malignant.

The clinical behavior and histologic features of this lesion do not favor classification of the lesion as a neoplasm. The only clinical characteristic which suggests neoplasia is the observation that the defect can increase in size. Whether this occurs independently of

a b

FIG. 12. Roentgenograms of distal tibia of 11 year old female, showing typical lesion. Curettement and bone grafting were performed. b, One year later, ossification of lesion.

a concomitant skeletal growth acceleration, and actually represents proliferation of the lesion has not been ascertained; but Lichtenstein has observed one defect which he claims nearly quadrupled in size within 2 years. Histologically there is no more evidence of neoplasia than is encountered in such lesions as lipomas or hemangiomas, both of which are considered by many pathologists to be developmental defects. Furthermore, there is no tendency for this lesion to undergo malignant transformation; and it is likely that in the rare case believed to have done so, the lesion was malignant in the beginning. Spontaneous healing has been frequently observed, strong evidence against neoplasia.

FIG. 13. Roentgenograms of a 17 year old patient whose first symptom was a fracture through the lesion incurred by minimal trauma while hurdling. After the fracture healed, the lesion was curetted and packed with bone.

A traumatic origin cannot be convincingly supported. It is unlikely that the defects would be so consistent in their skeletal location; that they would occur in protected areas such as the *lateral* aspect of the distal tibia; that they would occur with no history of significant injury; or that they would appear, disappear, and reappear again, if they were due to trauma. The fact that they *precede* fractures rather than follow them is also strong evidence against a traumatic origin. From a histologic study, little help is gained, for it is difficult to determine accurately either the significance or the interrelationships of the different components of the lesion. It is conjecture which came first: the fibrous tissue, the giant cells, the hemorrhage, or the xanthoma cells, and

Case	Age	Sex
1	10	M
2	16	F
3	15	M
4	12	M
5	12	F
6	11	M
7	18	F
8	16	F (c)
9	13	M
10	21	M
11	12	M
12	18	M
13	17	M
14	12	F
15	19	M
16	12	M
17	12	M
18	13	F
19	11	M
20	10	F

TABLE I.—DATA ON 20 CASES OF NONOSTEOGENIC FIBROMA OF BONE

Case *Age* *Sex*	*Skeletal location*	*Coexisting skeletal lesions*	*Initial symptom*	*Preop.*	*Surgical procedure*	*Follow-up*
1 10 M	Distal tibia	None	None	Bone cyst	Curettement and bone chips	2 yrs. No rec.
2 16 F	Distal femur	None	Persistent knee pain following trauma	Bone cyst	Excision	None
3 15 M	Proximal tibia	None	Fracture through lesion	Fibrous dysplasia	Curettement and bone chips	None
4 12 M	Distal femur	Osgood-Schlatter's disease	Pain over tibial tubercle	Benign giant cell tumor	Curettement and bone chips	None
5 12 F	Distal tibia	None	None	Bone cyst	Excision	3 yrs. No rec.
6 11 M	Distal tibia	None	Incidental finding sprained ankle	Nonossifying fibroma	Curettement	1 yr. No rec.
7 18 F	Proximal tibia	None	Fracture fibula; no prior symptoms	Xanthoma	Curettement	1 yr. No rec.
8 16 F (c)	Proximal tibia	None	Comp. fracture tibia; no prior symptoms	Fibrocystic disease	Curettement and bone chips	None
9 13 M	Distal femur	None	Dull aching pain, followed by fracture through lesion	Giant cell variant of bone cyst	Curetted; packed with bone chips	4 yrs. No rec.
10 21 M	Distal femur	None	Persistent pain following twisting injury to knee	Fibroxanthoma	Curettement implantation vastus medius muscle	4 yrs. No rec.
11 12 M	Distal tibia	None	Fracture through lesion	Giant cell tumor of bone	Excision and packing with bone chips	1 yr. No rec.
12 18 M	Proximal tibia	Osteochondroma opposite tibia	None	Nonossifying fibroma	Excision	6 mos. No rec.
13 17 M	Distal tibia	None	Fracture through lesion	Fibrous dysplasia	Curettement and bone chips	1 yr. No rec.
14 12 F	Distal fibula	None	Fracture through lesion	Bone cyst	Resection fibula; sliding bone graft	3 yrs. No rec.
15 19 M	Distal fibula	None	Aching pain lower leg	Osteoid osteoma	Excision	None
16 12 M	Proximal tibia	None	Pain over pes anserine bursa	Nonossifying fibroma	Excision	2 yrs. No rec.
17 12 M	Distal femur	Bipartite patella	None	Possible osteogenic sarcoma	Excision	3 yrs. No rec.
18 13 F	Proximal tibia	None	None	Nonossifying fibroma	Excision	2 yrs. No rec.
19 11 M	Distal femur	None	None	(Observed 3 years—some equivocal increase in size. . . .)		
20 10 F	Distal tibia	None	Fracture through lesion			1 yr. No change

cholesterol deposits. Any one or all of these may be concerned with the healing phase of any lesion involving hemorrhage, inflammation of trauma, or even the late stages of local bone infection.

We believe that this lesion is most likely a developmental defect, possibly belonging to the hamartoma group of lesions. However, in this respect it is entirely a local condition, self-limited in nature, and completely cured by adequate local excision. In this respect, it must be carefully distinguished from fibrous dysplasia, unicameral bone cysts, and other more poorly understood benign lesions of bone which have a strong tendency to recur. One should be able to do this easily on the basis of adequate roentgenograms and other features set forth in this article. If there is doubt, then the lesion is probably not a nonosteogenic fibroma; and biopsy verification is necessary.

Despite the conviction that these lesions are developmental, probably representing a focal dysplasia, the authors prefer the term nonosteogenic fibroma, or nonossifying fibroma. In the first place, the term has gained considerable popularity and is convenient to use; secondly, the defect is a fibrous lesion which does not produce bone. It is again emphasized that the term is employed to include all types of "metaphyseal fibrous defects." We believe that the phrase "metaphyseal fibrous defect," though descriptive, does not imply sufficient diagnostic specificity.

TREATMENT

Each lesion must be treated individually. If one is dealing with a typical metaphyseal defect, its mere presence is not necessarily an indication for surgery. Those which produce symptoms, those which are unusually large, and those through which a fracture has occurred should be removed. Small, symptomless lesions which do not increase in size may be observed at intervals without great concern; but it is essential that one be thoroughly familiar with the radiographic picture in order to decide which may be safely left alone. If there is any doubt, excisional biopsy should be accomplished.

Those lesions which are subject to surgery should be excised en bloc or curetted thoroughly. The defect, if significant in size, should be packed with bone chips in order to hasten healing and promote future strength of the bone (Fig. 12a and b). In the fibula, a lesion may be removed by segmental resection without bone grafting provided that it is not too near the ankle or knee. Postoperative x-ray therapy is neither necessary nor advisable, and it may be harmful.

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CORRELATION OF THE PATHOLOGIC AND RADIOGRAPHIC FINDINGS IN TUMORS AND PSEUDOTUMORS OF THE GALLBLADDER

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AT VARIOUS CONFERENCES in which the radiologist or pathologist participates, a question is sometimes raised concerning the significance of small intraluminal and nonopaque tumors of the gallbladder, often referred to as "papillomas" in the cholecystogram. The internist questions the symptomatology and the relation to gallbladder disease. Both internist and surgeon are concerned with the possible relationship of these small lesions to malignant disease. Our interest has, therefore, been stimulated to review not only our material but to survey the literature on the subject of benign gallbladder tumors.

Kirklin (1) in 1931 is credited with directing attention to papillomas of the gallbladder in cholecystograms. This article cites an incidence of 8.5 per cent of papillomas collected from 17,000 surgically removed gallbladders. Phillips reported on 500 gallbladders containing papillomas in 1933. Shepard, Walters, and Dockerty, reviewed the pathology of 150 benign neoplasms gathered from cases at the Mayo Clinic between 1906 and 1938. In addition to these, the literature is interspersed with numerous isolated case reports commenting on these tumors more or less as oddities. In our experience, and by employing our techniques, these lesions were found to occur with significantly greater frequency than ordinarily reported.

We have not been able to find a clear-cut histopathologic classification of structural changes in the gallbladder, neoplastic or otherwise. Nor is there adequate documentation of histologic criteria for accurate diagnosis of benign tumors and especially for differentiation from inflammatory and metabolic changes. The terminology has been ambiguous, accompanied by a wide variance in reported incidence and interpretation of the natural history of these lesions. As a result, clinical evaluation of radiographic findings is inconsistent.

Our purpose is to present an evaluation of focal elevated structures in the gallbladder based upon combined radiologic and pathologic study. Specifically, it includes a proposed classification of grossly demonstrable intraluminal lesions of the gallbladder, a correlation of the radiographically demonstrable lesions with their gross and microscopic pathology, and a suggested clinical approach.

In order to reconcile the wide divergence of incidence and interpretation, the necessity for uniform criteria and terminology becomes apparent. The following classification has been found useful for purposes of this study:

Proposed classification	*No. of cases in 1,000 gallbladders removed*
1. Epithelial tumors	
A. Papilloma	3
B. Adenoma	4
C. Carcinoma	12
2. Mesenchymal tumors	1
3. Pseudotumors	
A. Cholesterol polyp	16
B. Inflammatory polyp	4
C. Cholecystitis glandularis, proliferans	3
D. Congenital malformations	5

Papilloma. The term papilloma is limited to focal epithelial proliferations fulfilling the usual criteria for a benign true neoplasm. These tumors have a distinct pedicle or

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FIG. 1.

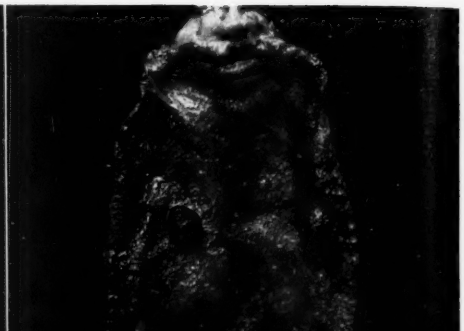

FIG. 2.

FIG. 1. Papilloma. Cholecystogram demonstrates a single stationary, ovoid, intraluminal lesion in gallbladder showing good concentration without stones.
FIG. 2. Solitary sessile papilloma. Fine lobulations can be seen grossly.

base and are composed of a fine, branching, vascular connective tissue stalk, supporting epithelium derived from gallbladder mucosa. The gross appearance closely resembles

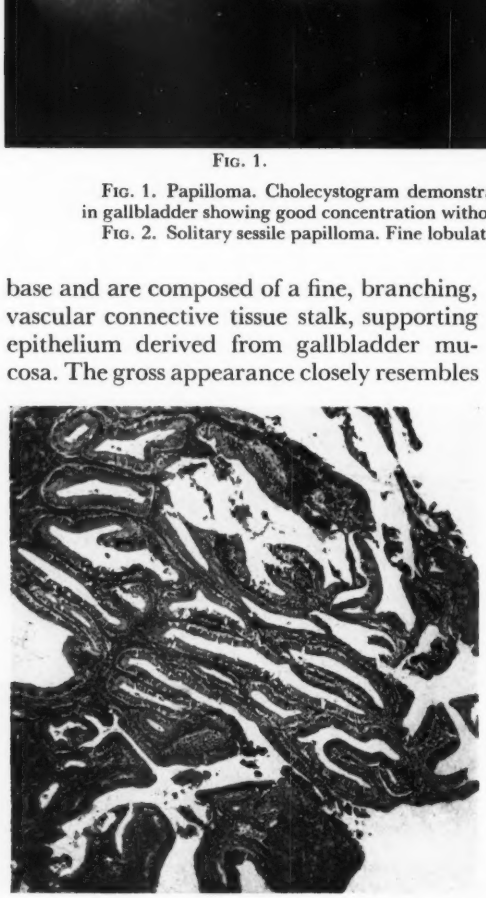

FIG. 3. Photomicrograph of lesion shown in Figure 2. Fine branching vascular stroma supports uniform columnar cells in this benign papilloma.

a papillary tumor of the urinary bladder as a soft, delicately branching, sessile or pedunculated structure, varying in color from tan to bright red. Because of its soft consistency, it is usually not palpable through the gallbladder wall. Histologically, the structure may follow a simple or complex villiform pattern. The epithelium is identical to that of normal biliary tract. Atypical proliferative activity may be encountered paralleling the changes in epithelial tumors of the colon. Diffuse papillary tumors may involve a large proportion of the mucosal surface. Infiltration of the stalk or base has been noted in our material and in other reported cases. These tumors thus fulfill all known criteria for epithelial neoplasms which may undergo malignant transformation (Figs. 1 to 5).

Adenoma. These tumors in the strict usage of the term should arise solely in the infundibulum, this being the only area in the gallbladder where glands normally occur. The presence of such tumors elsewhere may be explained by a misinterpretation of com-

plex papillary structures or by the presence of aberrant glands. Until large series are studied any difference in the natural history of the adenoma from that of the papilloma must be purely speculative. The cases studied by us suggest a tumor comparable to the adenoma of colon in gross and microscopic structure and in progressive alterations in the direction of malignant tumor. Grossly, they may be sessile or pedunculated, soft, red to grey in color, with a smooth velvety surface. Their soft consistency usually prevents palpation through the gallbladder wall. Histologically they are composed of closely packed glandular or tubular structures whose sparse stroma is not oriented into the branching pattern of papilloma. Active secretion by the cells will cause them to assume the goblet shape of mucous cells found in adenomas of colon. In some of these, reticulum stains may clarify the stromal architecture. Histologic alterations in these glandular tumors indicative of malignant transformation have been noted in our study and are reported by others. Here again, the changes closely parallel adenomas of colon. One gallbladder in our series contained an infiltrating carcinoma with several satellite adenomatous polyps. Differentiating between these tumors would appear justified because of the variation in behavior of papillary and adenomatous lesions in other viscera (Figs. 6 to 10).

Carcinoma. Carcinoma of the gallbladder has been well documented and is not further discussed here except to indicate that a high percentage of infiltrating carcinoma is associated with a residual unchanged papillary or adenomatous structure.

Cholesterol polyps. The cholesterol polyp is histologically an exaggerated focus of cholesterosis and consists of large collections of lipid laden macrophages beneath the basement membrane of the epithelium. The overlying epithelium is simple columnar or cuboidal and may show degenerative changes. The collections of macrophages produce a sessile or pedunculated tumefaction. They may be identified grossly as small

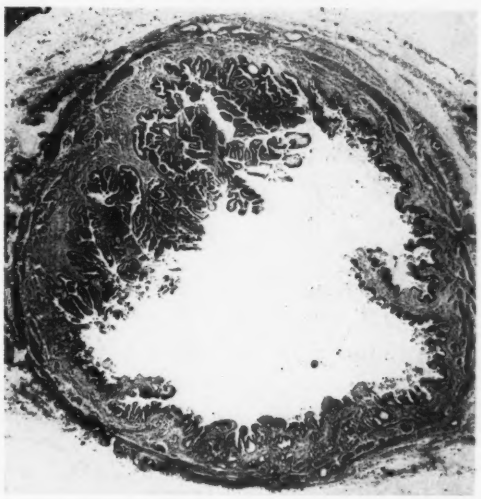

FIG. 4. Diffuse superficial papillomatosis. (Gallbladder nonfunctioning by x-ray examination).

pale yellow to white, opaque, mulberry-shaped structures, usually multiple and often associated with yellow mulberry-shaped cholesterol calculi identical in gross appearance to the attached structures. Cholesterol polyps are occasionally associated with diffuse cholesterosis. Their diameter may range

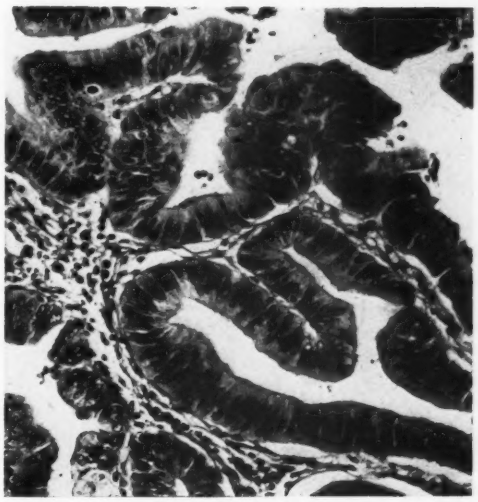

FIG. 5. Higher magnification of tumor in Figure 4. The architectural distortion and pleomorphic columnar cells fulfill usual criteria of noninfiltrating carcinoma.

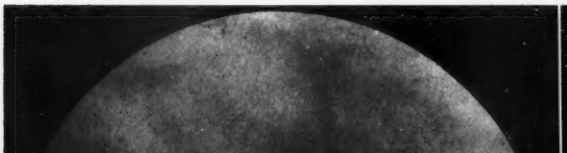

FIG. 6.

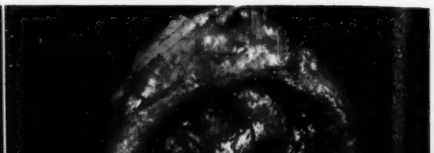

FIG. 7.

FIG. 6. Adenomatous polyp. Lateral decubitus cholecystogram. A poorly delineated intraluminal lesion (arrow) is seen adjacent to large nonopaque stone in gallbladder with satisfactory concentrating ability.

FIG. 7. Broad sessile adenomatous polyp (arrow).

from 1 to 6 millimeters, rarely larger (Figs. 11 to 16).

Inflammatory polyps. The inflammatory polyp is differentiated here from the proliferative changes seen in cholecystitis glandularis proliferans because it is solitary or occurs as 2 to 3 discrete lesions unaccompanied by diffuse proliferative changes. The distinction is probably artificial, but when solitary, the problem of differentiation from true epithelial tumors arises. These polyps are usually rather firm, 3 to 6 millimeter, sessile structures which may resemble pyogenic granuloma or they may have a firm, pale greyish color depending upon the degree of fibrosis. Histologically the stroma of these structures is usually abundant, edematous, containing fine, distended capillary channels, often suggesting granulation tissue. The stromal fibrils are disoriented, short, coarse and fragmented, often hyalinized, in contrast to the well oriented, delicate stromal fibers of the adenoma and the oriented single vessels and branching stromal structure seen in the papilloma. Significant inflammatory infiltrate and occasional hemorrhage are present in the supporting tissue. Superficial erosion is almost constant

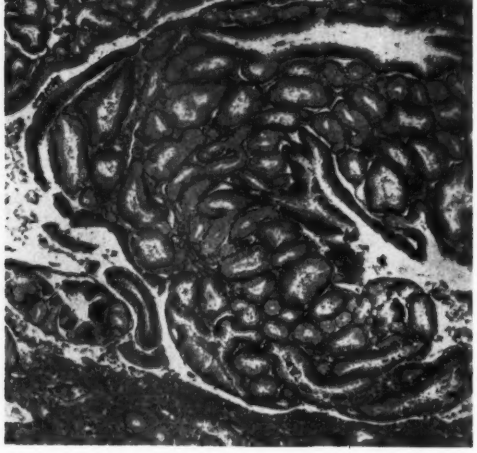

FIG. 8. Tubular and glandular structure of the adenomatous polyp. Resembles adenomatous polyps of colon.

in the inflammatory polyp, and the remaining epithelium is pale, acidophilic, showing degenerative alterations. Proliferative activity in the epithelium is seldom seen although in areas of erosion alteration in cells suggest regenerative activity (Figs. 17 to 19).

Cholecystitis glandularis proliferans. Pseudopolyps and raised intraluminal structures are often seen in cholecystitis glandularis proliferans. This is always a diffuse inflammatory lesion accompanied by significant mural thickening of the gallbladder and a coarse granular mucosal surface. The elevated structures are multiple, sessile, firm, 3 to 6 millimeters in diameter. When seen they may be difficult to differentiate grossly from early infiltrative carcinoma and sections must be taken for identification of the process. Histologically the raised structures are often seen to be the result of cystic islands of mucosa incorporated in scar. It is at once apparent in the epithelial elements that spontaneous proliferative activity is not present but that this lesion represents distortion and reduplication of gallbladder epithelium.

Anomalies. By far the most common anomaly of development which produces a demonstrable tumefaction in the gallbladder is the entity commonly termed "adenomyoma." This lesion is characteristically in the fundus of the gallbladder, producing a lentiform eminence covered by grossly normal mucosa. Many exhibit central mucosal umbilication. In microscopic sections one sees cystic structures or a maze of narrow epithelium-lined slits surrounded by trabeculae of smooth muscle. In some, the smooth muscle is oriented around the spaces and the fibers may be seen coursing in the direction of and into adjacent gallbladder muscle. Some of these structures are entirely external to the normal muscularis. In cases serially sectioned, cystic spaces often communicate with the gallbladder lumen. The lining epithelium of cysts is identical to that of the gallbladder mucosa. We have chosen to call these *myoepithelial anomalies* having origin in the failure of orientation of cells in the tip of the primordial gallbladder bud. Because they arise in the fundus of the gallbladder, a frequent focus of primary carcinoma of this structure, they may be mistaken at gross examination for fundic carcinoma (Figs. 20 to 25).

FIG. 9. Adenomatous polyp. Higher magnification. Goblet type cells are clearly shown.

Other malformation. Cystic Aschoff-Rokitansky sinuses containing calculi (mural cal-

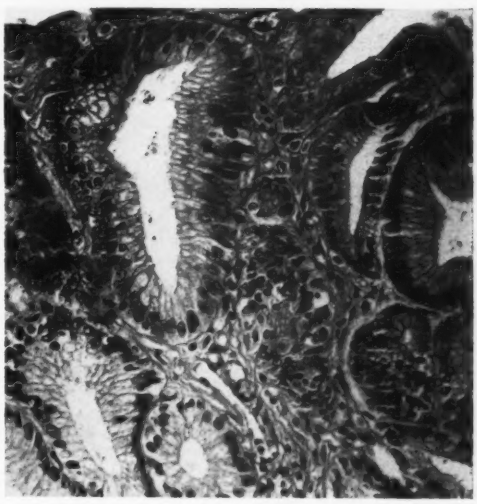

FIG. 10. Adenomatous polyp. Increased proliferative activity in glandular element comparable to changes in adenomatous polyps of large bowel.

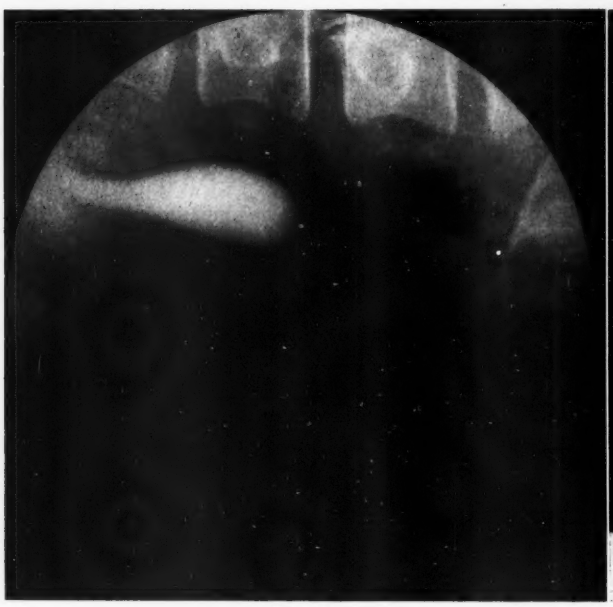

FIG. 11.

FIG. 12.

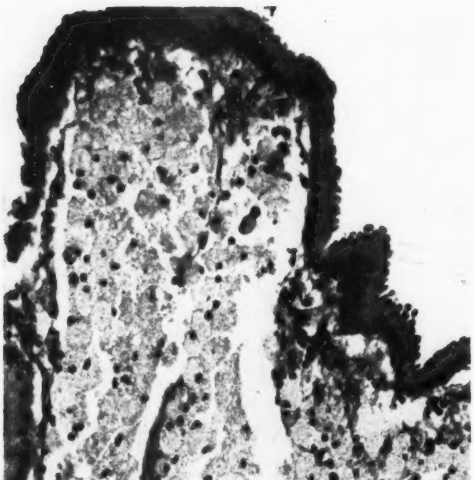

FIG. 13.

FIG. 11. Cholesterol polyps. Cholecystogram. Multiple discrete intraluminal lesions varying in size scattered throughout gallbladder.

FIG. 12. Typical white to yellow mulberry appearance of cholesterol polyps. Many of these are attached by a delicate pedicle easily detached. They may be associated with mulberry, cholesterol or mixed stones identical in shape to residual cholesterol polyps.

FIG. 13. Cholesterol polyp. Uniform epithelium with lipid-laden macrophages beneath basement membrane.

culi) may rarely produce a significant elevated mucosal lesion.

Radiographic findings. We have been unable to differentiate in all instances papillomas, adenomas, inflammatory polyps, and cholesterol polyps on the basis of cholecystographic examination. All are single or multiple, sessile or pedunculated. Certain characteristic differential features are, however, of value for generalization. The papilloma is usually a discrete single lesion as seen on the cholecystogram and tends to be flat or sessile in contrast to multiple cholesterol polyps. The adenoma is likewise characteristically a solitary tumor, often pedunculated with the appearance in the cholecystogram of a small spherical, intraluminal body which is translucent. Cholesterol polyps appear as well delineated translucencies, usually multiple and spherical because of their narrow pedicles. When multiple their diameters vary from 1 to 6 millimeters, rarely larger. An important differential feature of the cholesterol polyp is the unusually intense ability of the gallbladder to concentrate. This finding is in agreement with the

FIG. 14.

FIG. 15.

work of Kirklin, Caylor, and Bollman who found that gallbladders bearing these lesions and associated hypertrophic rugae produced the greatest concentration of bile. We have followed 1 case as long as 3 years without recognizable change in size and number of the cholesterol polyps and no change in concentrating ability.

The inflammatory polyp exhibits no unusual radiographic findings to characterize it from other tumescences. When solitary it may resemble papilloma or adenomatous polyp and although more frequently associated with impaired function and cholelithiasis, this is not a valid differential feature in an individual case.

The papilloma, the adenomatous polyp, and the inflammatory polyp must be, for practical purposes, then grouped together as intraluminal lesions, usually solitary, less sharply outlined than the cholesterol polyps, and more frequently associated with coexistent gallstones and with gallbladders showing a slightly diminished ability to concentrate.

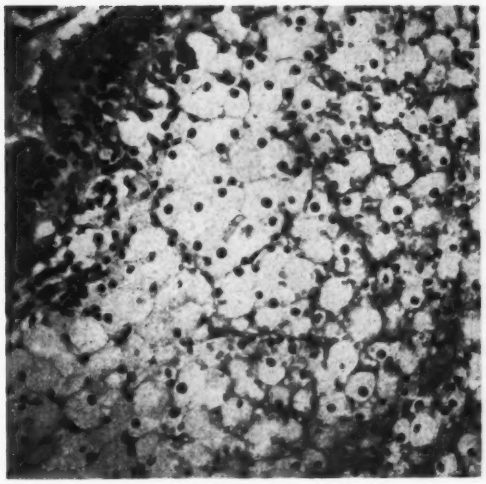

FIG. 16.

FIG. 14. Cholesterol polyp. Cholecystogram. Solitary, well defined intraluminal defect remaining in constant position.

FIG. 15. Solitary cholesterol polyp. Pale yellow color is key to gross identification.

FIG. 16. Cholesterol polyp. Macrophage element may show histologic variation dependent upon physical state or chemical composition.

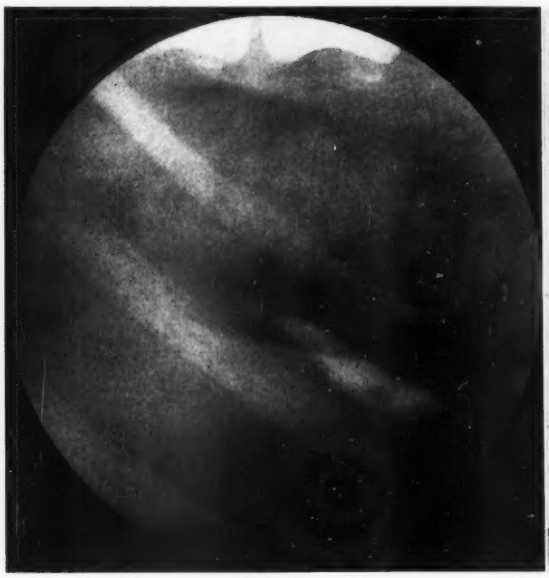

FIG. 17.

FIG. 18.

FIG. 17. Inflammatory polyp. Cholecystogram. Angular, nonmobile lesion usually larger than cholesterol polyp.

FIG. 18. Hemorrhagic lesion with smooth surface. Contours typical of inflammatory pseudopolyp.

The myoepithelial anomaly produces a characteristic deformity on the cholecystogram. These are considered curiosities which are always found in the fundus and produce a lentiform invagination with distortion of the normal rounded contour of that portion of the gallbladder. They show varying degrees of central umbilication of the mucosal surface. The deformity they produce must be constantly demonstrated in several views to substantiate their presence and to exclude pressure deformities caused by extrinsic sources.

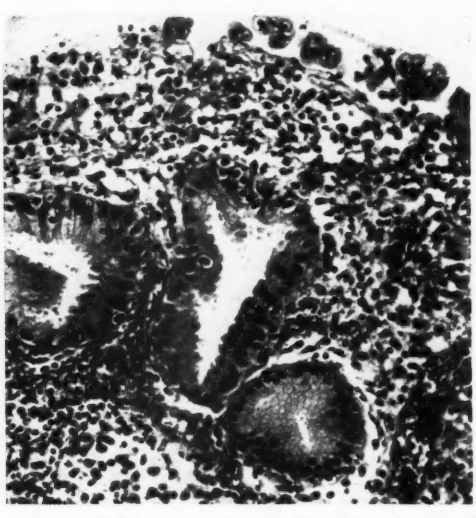

FIG. 19. Inflammatory pseudopolyp. Degeneration of surface epithelium, inflammatory infiltrate, and random architecture are noteworthy.

The diffuse involvement of the gallbladder mucosa in cholecystitis glandularis proliferans is usually sufficient to render a radiographically nonfunctioning gallbladder; therefore, this condition cannot be included in the differential diagnosis of demonstrable lesions.

RADIOGRAPHIC TECHNIQUE

The detection of intraluminal defects in the gallbladder is relatively simple but still requires rather meticulous radiographic technique. It is our procedure to take at least 2 of the films of the cholecystographic series in the right lateral decubitus position. After a lateral decubitus posteroanterior

FIG. 20.

FIG. 21.

FIG. 20. Myoepithelial anomaly. Cholecystogram. Lentiform invagination of wall at tip of fundus, characteristic of this anomaly.

FIG. 21. Its location in fundus and gross appearance suggest anomalous failure of complete expansion of primitive gallbladder bud in myoepithelial anomaly.

projection is taken cholex® or similar cholagogue is given. Within 10 minutes the second film is taken, again in the lateral decubitus position. By this time the first film has been sufficiently processed for "wet viewing" by the radiologist. He suggests necessary modifications of technique and further films that may be necessary to clarify any problem. As a rule, we find in the nonproblem case 2 films sufficient for the entire examination. Spot films taken at fluoroscopy are employed with the patient in the erect position, whenever the lateral decubitus positioning is not satisfactory. This is a rare occurrence in our department.

The technique used by us differentiates readily between multiple small nonopaque stones and intraluminal tumors. Stones invariably will "layer out" in the lateral decubitus position while polyps, papilloma, and other tumors will ordinarily hold their position. Any slight change in their position is attributed to shift in the gallbladder wall and mobility because of attachment to a thin pedicle in some instances.

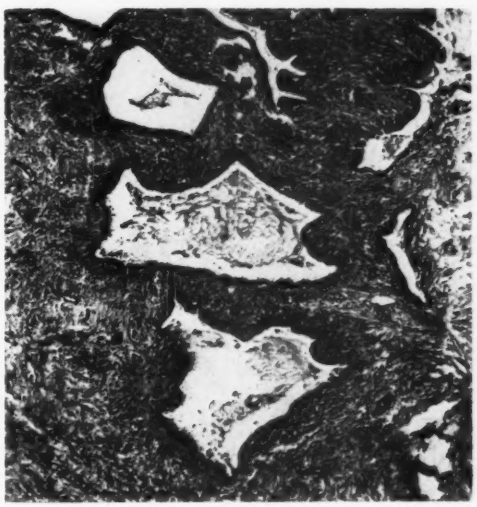

FIG. 22. Myoepithelial anomaly. Epithelium-lined cysts surrounded by well developed zone of smooth muscle.

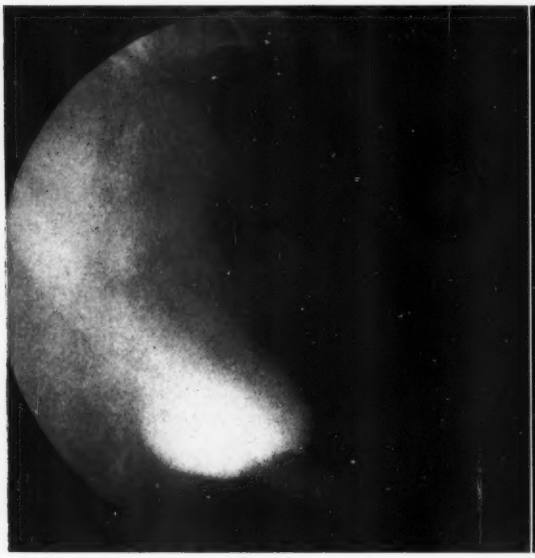

FIG. 23.

FIG. 24.

FIG. 23. Myoepithelial anomaly. Almost identical radiographic appearance as Figure 20. Stone also present.

FIG. 24. Invaginated "button" structure of some myoepithelial anomalies may simulate infiltrating carcinoma.

Discussion. The past literature for the most part has tended to discount as unimportant demonstrable intraluminal nonopaque tumors of the gallbladder. Lack of clear-cut criteria for classification has lumped these tumors into a general "wastebasket" called "papilloma," considered to be entirely benign and not to constitute an indication for cholecystectomy. Our own experience and the experience of others leads to the conclusion that some of these must be classified as true epithelial neoplasms with malignant potential. Accurate classification of large series may contribute to our knowledge and natural history of gallbladder cancer. It is our opinion that until more definite criteria are developed to differentiate preoperatively benign intraluminal inflammatory or metabolic lesions from true epithelial neoplasms, the finding of solitary small intraluminal, nonopaque tumors on the cholecystogram alone constitutes an indication for cholecystectomy. One should be cautioned against jumping to conclusions on the basis of a single examination. The demonstration of any nonopaque intraluminal lesion must be confirmed by repeat procedure carrying

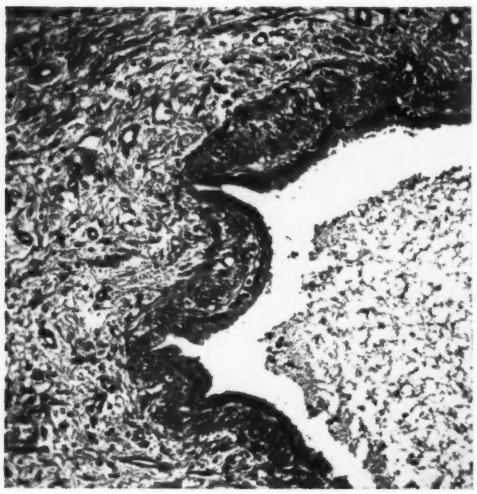

FIG. 25. Oriented smooth muscle zone around cystic spaces is a characteristic feature of the myoepithelial anomaly.

out any special technique that may be desirable.

CONCLUSIONS

1. Intraluminal, nonopaque tumors of the gallbladder deserve accurate histologic classification as the basis for further study of large series.

2. Meticulous cholecystography with precise histologic classification should yield more accurate preoperative diagnoses.

3. It has been shown conclusively that some lesions are true epithelial neoplasms and will show malignant transformation. It follows, therefore, that a solitary, radiographically unclassifiable tumor of the gallbladder constitutes an indication for cholecystectomy.

4. The term myoepithelial anomaly more accurately reflects the true nature of the fundic lesion which has been previously referred to as adenomyoma. These lesions are clinically insignificant.

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STUDY OF SERUM PROTEINS WITH PAPER ELECTROPHORESIS

Part II. Observations on Serum Protein Fractions in Patients Undergoing Hypothermia During Intracranial Surgery

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BLOOD CHEMISTRY DETERMINATIONS during hypothermia in the course of intracranial operation have revealed progressive reductions in hemoglobin, hematocrit, and total serum protein. Failure of adequate blood replacement during the operative procedure was suggested as the cause of these changes. The investigation here reported was devoted to a study of the changes in the serum protein fractions that occurred during and after hypothermia in 3 patients undergoing intracranial operation.

MATERIAL AND METHODS

We have previously recorded in greater detail the clinical histories and described the hypothermia of the patients in this study (1). Cerebrospinal fluid pressure measurements were made during and following surgery with a Tuohy continuous spinal catheter in the lumbar intrathecal space.

Serum protein specimens were taken during the preoperative period, during the lowest temperature of the patient, and at intervals during the postoperative period. Ten lambda aliquots of undiluted serum and serum diluted to an approximate 3 grams per cent level were employed in the paper electrophoretic separations. Eight electrophoretic determinations were made of each diluted and undiluted serum specimen and the means of these determinations are recorded in the graphs in grams per cent and dye units as previously described (2, 3).

Variance analyses of the mean dye unit data of albumin, alpha-1 and alpha-2 globulin fractions were performed on the 3 grams per cent serum dilution, and comparative studies during the postoperative period were made with the preoperative determinations. Conversion of the dye unit data of the albumin in this serum dilution to grams per cent albumin data was made according to graph 2 of a previous study (3) in which a relationship between dye units and grams per cent of electrophoretically separated albumin was demonstrated. The numerical values obtained in these conversions are considered an index of the absolute grams per cent of the albumin fraction in the serum.

CASE REPORTS

CASE 1. This 54 year old male had neurologic symptoms and diagnostic studies which indicated a right occipital space-occupying lesion.

Under hypothermia an incomplete removal of an infiltrating glioma was carried out by a right occipital lobectomy. The superior longitudinal sinus was entered and massive venous hemorrhage occurred. Cerebrospinal fluid pressure, temperature, and blood pressure during operation were recorded in a previous study (1). The patient was given 3,500 cubic centimeters of blood during the operative procedure. Preoperative hemoglobin determination was 13 grams per cent; this determination on the third postoperative day was 11 grams per cent, and on the tenth postoperative day it was 9.5 grams per cent.

Figure 1 demonstrates the decrease in total serum protein and total serum albumin which occurred on

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the first postoperative day. Statistical study of the 3 grams per cent serum dilutions revealed that changes occurred during the postoperative period which were characterized by a decrease in albumin on the first and third postoperative days, by an increase in alpha-2 on the third and seventh postoperative days, and by an increase in alpha-1 on the seventh postoperative day (variance analysis: $p < .01$ level). This same pattern was demonstrated in the total quantity of these fractions in the graph of the undiluted serum.

CASE 2. This 24 year old male had had an incomplete removal of a right parietal parasagittal tumor. Neurologic symptoms and diagnostic studies indicated a massive recurrence of the tumor.

Under hypothermia a recurrent malignant ependymoma was removed from the right frontoparietal area, along the falx, convexity of the right frontal lobe, and floor of the anterior fossa. An incision was made into the region of areas 6 and 8 and a subcortical decompression of the right frontal lobe was made from this point forward. The cerebrospinal fluid pressure, rectal temperature, and blood pressure during and after operation are recorded in Figure 2.

For 2 days preoperatively the patient received an intravenous infusion each day of 1,000 cubic centimeters of 5 per cent glucose in water and 1,000 cubic centimeters of 5 per cent glucose in normal saline. On the day of operation the patient received 500 cubic centimeters of 5 per cent glucose and 1,500 cubic centimeters of whole blood intravenously and 300 cubic centimeters of water orally. The patient was incontinent and accurate output was not determined. On the first postoperative day he received 1,500 cubic centimeters of 5 per cent glucose in water and he was incontinent on this date. The second postoperative day he was given 1,000 cubic centimeters of 5 per cent glucose, 1,000 cubic centimeters of isotonic saline intravenously plus 250 cubic centimeters of water orally. Urinary output was 1,610 cubic centimeters. One hundred cubic centimeters of a 25 per cent solution (25 gm.) of normal serum albumin (human) was administered at 5:30 p.m. on the second postoperative day. On the third postoperative day he was given 1,000 cubic centimeters of 5 per cent glucose in water intravenously and 400 cubic centimeters of water orally. Urinary output was 800 cubic centimeters.

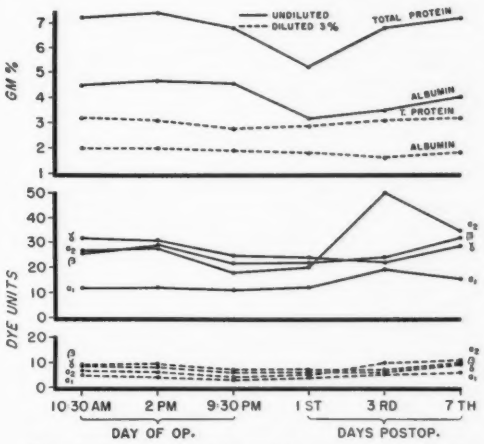

FIG. 1. Graph of total protein and paper electrophoretic serum protein patterns of undiluted serum and 3 grams per cent dilution of serum in Case 1 during hypothermia in course of intracranial operation.

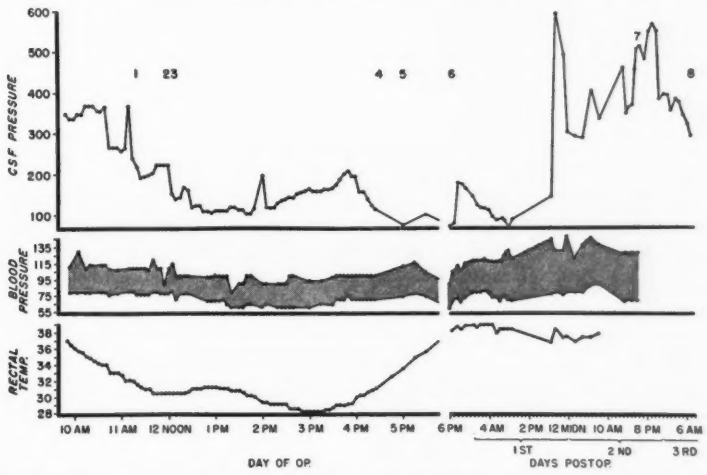

FIG. 2. Graph of rectal temperature, cerebrospinal fluid pressure, and blood pressure in Case 2 during and after hypothermia and intracranial operation: *1*, scalp incision; *2*, bone flap removed; *3*, dura opened; *4*, return to recovery unit; *5*, flat in bed; *6*, semi-Fowler's position; *7*, 25 per cent normal serum albumin (100 c.c.).

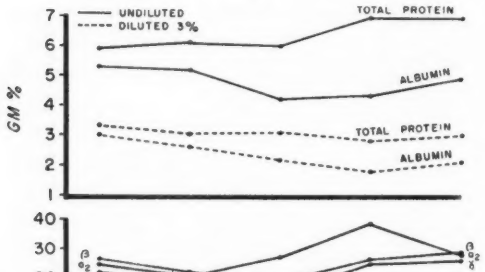

FIG. 3. Graph of total protein and paper electrophoretic serum protein patterns of undiluted serum and 3 grams per cent dilution of serum in Case 2 during hypothermia in course of intracranial operation.

Preoperative hemoglobin determination was 14.5 grams per cent; this determination on the first postoperative day was 10.5 grams per cent, and on the fifth postoperative day this was 9 grams per cent.

Figure 3 demonstrates that an increase in total serum protein occurred during the first postoperative week. A progressive decrease in total albumin occurred during the first postoperative week. Statistical analysis of the 3 grams per cent serum dilutions revealed that changes occurred during the postoperative period which were characterized by decrease in albumin in all determinations during the postoperative period and by increases in alpha-2 on the eighth and eleventh postoperative days. No statistical significant increase in alpha-1 occurred during the postoperative period (variance analysis: $p < .01$ level of significance). This same pattern was observed in the total quantity of these fractions as illustrated in the data of the undiluted serum. Figure 2 demonstrates the elevation in cerebrospinal fluid pressure on the second and third postoperative days.

CASE 3. This 60 year old male had neurologic symptoms of a space-occupying lesion in the right frontal lobe.

Under hypothermia a right frontal osteoplastic craniotomy was performed and neoplasm was found along the floor of the anterior cranial fossa extending across the midline. This tumor lay adjacent to the anterior cerebral arteries and the optic nerves and chiasm were compressed by neoplasm. Removal of tumor resulted in hemorrhage from the recurrent artery of Heubner and proximal anterior cerebral artery. Cerebrospinal fluid pressure, rectal temperature and blood pressure during and following operation are recorded in Figure 4.

The administration of 100 milligrams of hydrocortisone sodium succinate in 500 cubic centimeters of distilled water was started at 10:00 a.m. during operation. He was given 500 cubic centimeters of isotonic saline and 1,000 cubic centimeters of blood

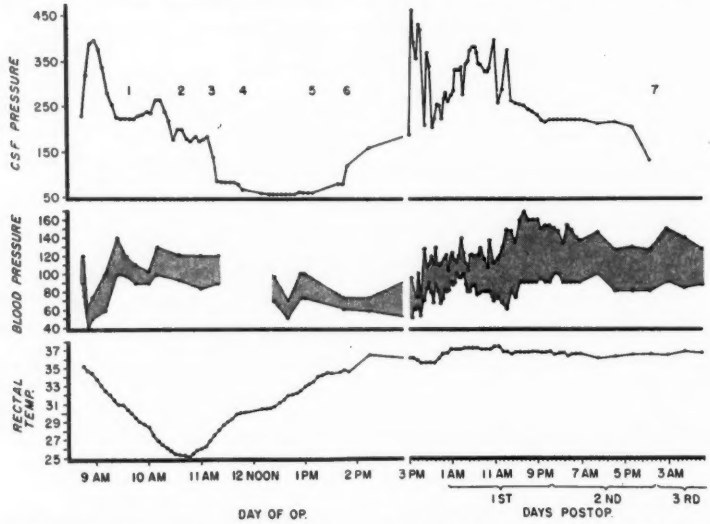

FIG. 4. Graph of rectal temperature, cerebrospinal fluid pressure, and blood pressure in Case 3 during and after hypothermia and intracranial operation: *1*, scalp incision; *2*, bone flap removed; *3*, dura opened; *4*, hemorrhage from anterior cerebral artery; *5*, surgery completed; *6*, return to recovery unit; *7*, catheter removed.

on the day of operation. On the first postoperative night the patient was given 100 milligrams of cortisone at 7:00 p.m., and on the first postoperative day he was given 100 milligrams of cortisone at 9:00 a.m. During the first postoperative day fluid administration included 1,000 cubic centimeters of 5 per cent glucose in water and 1,000 cubic centimeters of 10 per cent glucose in normal saline. During the second and third postoperative days fluid administration included on each day 1,000 cubic centimeters of 5 per cent glucose in normal saline and 1,000 cubic centimeters of 5 per cent glucose in water.

Figure 5 demonstrates that reductions in total serum protein and total albumin occurred in the immediate postoperative determinations. Statistical study revealed that changes in the 3 grams per cent dilution occurred in the immediate postoperative determination and first postoperative day determination characterized by increases in the albumin fraction and no significant changes in the globulin fractions. Increases in alpha-1 globulin fraction occurred on the second and sixth postoperative days and increase in alpha-2 globulin occurred on the sixth postoperative day (variance analysis: $p < .01$ level of significance). Decrease in globulin fraction was revealed in the immediate postoperative determination in the undiluted serum. Figure 4 shows elevation in cerebrospinal fluid pressure in the immediate postoperative period.

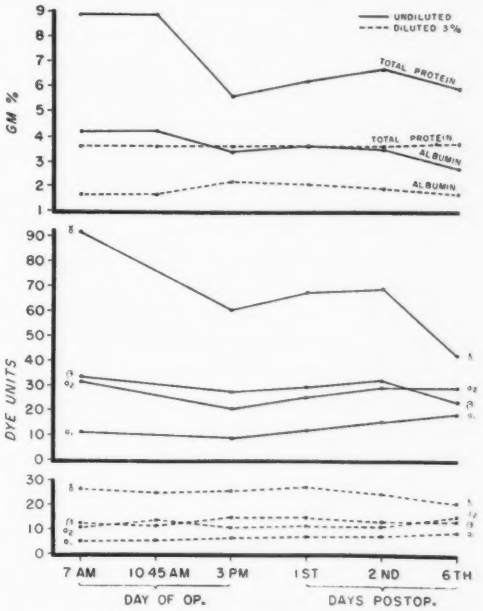

FIG. 5. Graph of total protein and paper electrophoretic serum protein patterns of undiluted serum and 3 grams per cent dilution of serum in Case 3 during hypothermia in course of intracranial operation.

DISCUSSION

Study of the metabolic response to craniotomy in the postoperative period have revealed sodium retention, potassium loss, nitrogen loss, and frequently oliguria; such trends are reversed in several days. This investigation did not include serum protein patterns following craniotomy, although such study in patients undergoing major surgery for a variety of other illnesses have revealed a decrease in serum albumin and increases in alpha-1 and alpha-2 globulin fractions. Each patient in this investigation following craniotomy had a decrease in serum albumin and an increase in alpha-2 globulin during the postoperative period. These observations conform with the metabolic response noted for surgery and do not appear incident to the hypothermia used.

Decreases in total serum protein determinations were found in 2 of the cases during the postoperative period following hypothermia in intracranial operation. In the other case no decrease was found in total serum protein, while a decrease in hemoglobin occurred in the postoperative period. This discrepancy suggests that changes are occurring in protein metabolism secondary to operation which are independent of a failure in blood replacement during surgery under hypothermia.

Preoperative comparisons of total serum protein and globulin fractions determinations revealed that they were higher in Case 3 than in the other 2 cases. A possible relationship of these protein changes in the former case to an effect of tumor on the hypothalamus has been suggested in experimental studies in animals. These investigations have revealed increases in globulin and total serum protein on stimulation of certain areas of the hypothalamus. In the postoperative period in this case, increase in dye units of albumin without change of globulin fractions or total protein suggested that an increase in stainability of albumin had occurred in the serum dilutions. This finding may be secondary to the hydrocor-

tisone administered during operation, inasmuch as protein patterns have been altered in experimental study following various hormone medications.

Observed changes in cerebrospinal fluid pressure in man have been related to a net shift of fluid into or out of the craniospinal extravascular fluid space as a result of unbalancing the hydrostatic and osmotic equilibrium across the walls of the craniospinal capillaries. Since serum albumin has a vital role in maintaining intravascular osmotic pressure in the blood-cerebrospinal fluid barrier, progressive decrease in serum albumin during the postoperative period could be reflected in the elevations in cerebrospinal fluid pressure noted in the 2 cases of this study. In this postoperative period the shift of fluid across the blood-cerebrospinal fluid barrier may be influenced by additional factors, such as: fluid balance of the patient, quantity and electrolyte content of administered intravenous fluids, and abnormalities in electrolyte metabolism. Administration of intravenous serum albumin in this period could not be measured by methods used nor was it reflected in any marked change in cerebrospinal fluid pressure.

Decrease in serum albumin occurred more rapidly in Case 3 and elevation in cerebrospinal fluid pressure developed in the immediate postoperative period. Involved in these observations may be the effect of operation and neoplasm on the region around the third ventricle. This was suggested in stimulation studies of the ventromedial hypothalamic nucleus in animals with resultant marked elevation of cerebrospinal fluid pressure and increase in cerebrospinal fluid protein. Another important factor in this case could be the metabolic effects of the administered steroids which may result in retention of sodium, chloride and water, with loss of potassium, and catabolism of body protein. Further study of hormone administration may reveal patterns of serum proteins and cerebrospinal fluid pressures which would improve the postoperative course after craniotomy under hypothermia.

SUMMARY

Total serum protein determinations and serum protein patterns of 3 cases of intracranial operation carried out under hypothermia are presented during the operative and postoperative period. A discrepancy in 1 case between total serum protein and hemoglobin determinations suggested that changes in protein metabolism were occurring independent of a failure in adequate blood replacement during operation under hypothermia. A decrease in total serum albumin and increase in alpha-2 globulin occurred in the postoperative period in all cases following craniotomy. These changes are not considered specific for hypothermia since similar patterns have been found in the postoperative period following major operation under general anesthesia. Cerebrospinal fluid pressure elevation occurred during the first 24 hour postoperative period in a patient treated with steroids who had a neoplasm removed from the region of the third ventricle. On the other hand, cerebrospinal fluid pressure elevation developed during the 24 to 36 hour postoperative period in a nonhormone treated case of tumor over the convexity of the cerebral hemisphere. Elevation in cerebrospinal fluid pressure coincided with a pattern of progressive reduction in serum albumin for a time in the postoperative course of these 2 cases.

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GLUCOSE POTENTIATION OF POTASSIUM ASYSTOLE

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THE SURGICAL APPROACH to the chambers of the heart can be achieved by extracorporeal pump oxygenation. A quiet operative field, completely free of blood, is an aim common to all surgery. At present, this prerequisite in cardiac surgery can best be achieved by the use of potassium induced cardiac asystole.

The concentration of potassium necessary to produce effective rapid cardiac arrest has been established as between 2½ and 10 per cent. A variety of substances has been used in combination with potassium to potentiate its action. These substances include magnesium sulfate, acetylcholine, and prostigmin. It is noted that the most effective cardioplegics always contain potassium. Melrose, in his preliminary communication on elective cardiac arrest, diluted a 25 per cent solution of potassium citrate with blood to attain the desired concentration. His choice of the use of blood as a diluent was not elaborated on. This article presents experimental evidence for the potentiation of potassium induced asystole by glucose, and its significance in defining the site of potassium citrate action.

After elective cardiac arrest has been carried out with potassium, the restoration of an effective heart beat has presented difficulties. These difficulties are primarily concerned with ventricular fibrillation and ineffective cardiac action. The use of a solution of sodium lactate in atrioventricular heart block has been described clinically by Bellet (1, 2). Its use experimentally after elective potassium arrest in hypothermia has been presented by Young and Schimert. The action of sodium lactate in these conditions has been postulated as due to alkalinity, increased conductivity due to the presence of the sodium ion, or the direct use of lactate by the heart for nutrition. This article presents evidence to substantiate the resuscitative effects of sodium lactate on the heart in standstill and its mode of action.

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METHOD

A bubble type pump oxygenator system was used to by-pass the heart. Blood was removed from the inferior and superior vena cava via catheters inserted through the right atrium. The blood was oxygenated and then returned to the dog via a catheter in the femoral artery. Mongrel dogs weighing between 12 and 22 kilograms were used for all experiments. The dogs were anesthetized with pentothal sodium intravenously, and an airway was maintained with a rubber endotracheal tube and an inflatable bag. Compressed air was used in the respirator. An umbilical tape was passed about the ascending aorta. This umbilical tape about the aorta was used only to elevate the aorta so that it could be occluded, injected, or sutured. One to 3 minutes after extracorporeal circulation was begun, the ascending aorta was clamped with a noncrushing arterial clamp, and 2½ per cent potassium citrate in 5 per cent dextrose and water was injected rapidly into the proximal aorta through a No. 19 needle until all cardiac action ceased. Right ventriculotomy was then carried out in all but 2 of the animals. Respiration was continued throughout the procedure. The ventriculotomy was closed and the aortic clamp was removed.

In the last 8 animals the ascending aorta was injected with 10 cubic centimeters of 10 per cent sodium lactate just before the aortic clamp was removed.

In approximately one-half of the animals, 200 cubic centimeters of blood were removed from the coronary sinus after opening the aortic clamp. This blood was discarded. In the remaining animals this blood was allowed to return to the oxygenator.

Following resumption of a normal heart beat the extracorporeal circulation was interrupted and, if an effective beat was observed, the caval catheters were removed.

Blood for determination of serum potassium levels was drawn from the experimental animals (1) before perfusion, (2) at time of asystole, and (3) at the time of resuscitation. The determinations of serum potassium were done by flame photometry and reported in milliequivalents per liter.

TECHNIQUE OF PRODUCING POTASSIUM ASYSTOLE

The flow in the aorta is retrograde after extracorporeal circulation is established and, therefore, an attempt was made to inject the potassium into the ascending aorta before clamping it. In this manner it was possible to cause cardiac arrest very promptly. However, as the excess potassium diffused to the aortic arch and carotid sinus, there was a massive attempt by the animal to respire and the chest moved so violently that injection of potassium into the aorta was at times difficult. This reaction was also observed when 10 per cent sodium lactate was injected into the ascending aorta without cross-clamping. These alkaline solutions appear to stimulate the chemoreceptors of respiration in the carotid sinus and aortic arch, resulting in an attempt by the animal to respire.

This syndrome was verified in 10 dogs and, consequently, we now clamp the aorta and inject potassium into the proximal aorta. After the aorta is clamped there is a very low pressure in the proximal aorta which results in opening of the aortic valve. If potassium is injected slowly it will, in a large part, be deposited in the ventricle and not aid in the production of asystole. Therefore, we find it necessary to inject potassium rapidly with a large caliber needle, in order to close the aortic valve and force the potassium into the coronary arteries.

If a large amount of potassium is allowed to run into the left ventricle through an open aortic valve on resumption of cardiac beat, the heart action will promptly be arrested again because of the forcing of blood with a high concentration of potassium into the coronary arteries.

RESULTS

In 9 animals (dogs 36 through 44), cardiac arrest was induced by injecting 7 to 12 cubic centimeters of potassium citrate in blood into the proximal aorta. Cardiac arrest was prompt in all cases and recovery did not occur until the coronary arteries were perfused with oxygenated blood (Table I).

In 14 animals (dogs 45 through 58), 2.5 per cent potassium citrate in 5 per cent glucose solution was injected in the proximal aorta. In all cases cardiac arrest was prompt, and recovery did not occur until the coronary arteries were perfused with oxygenated blood (Table I).

In 5 animals (dogs 51 through 55), 2.5 per cent potassium citrate in normal saline was injected into the proximal aorta. In all cases, cardiac arrest was prompt; however, a regular cardiac rhythm returned within 1 minute without perfusion of the coronary arteries or any other resuscitative measures (Table I). These animals' hearts subsequent to a short period of coronary perfusion were placed in prolonged asystole by using potassium citrate in 5 per cent glucose as a cardioplegic and are included in that group also.

In 3 animals (dogs 56 through 58), 2.5 per cent potassium citrate was injected into the proximal aorta. In these cases, cardiac arrest was prompt; however, a regular

TABLE I.—EFFECT OF DILUENT UPON DURATION OF POTASSIUM ASYSTOLE

	2.5 per cent potassium citrate in saline	*2.5 per cent potassium citrate*	*2.5 per cent potassium citrate in blood*	*2.5 per cent potassium citrate in 5 per cent glucose*
Average length of asystole	60 seconds in 5 experiments	3 minutes in 3 experiments	23 minutes in 9 experiments	25 minutes in 14 experiments
Spontaneous escape from effects of potassium without coronary perfusion	Yes	Yes	No	No
Amount of mixture needed to cause asystole, c.c.	7–10	7–20	7–12	4–15

Injection of potassium was stopped as soon as cardiac arrest had been achieved.

TABLE II.—POTASSIUM LEVELS WITH RECIRCULATION OF CORONARY SINUS BLOOD

Dog No.	*Venous blood before cardiac arrest*	*Venous blood immediately after induction of cardiac arrest*	*Venous blood after resuscitation of the heart*
53	4.6	6.8	4.5
57	3.7	6.9	5.0
58	5.1	5.9	4.8
59	4.2	5.0	3.9

All values are potassium concentration in milliequivalents per liter. In these experiments between 175 and 300 milligrams of potassium citrate were used to produce cardiac arrest.

TABLE III.—RESUSCITATION WITH SODIUM LACTATE

Dog No.	*Ventricular fibrillation*	*Recovery time from release of aortic clamp, mins.*	*Animal survival*	*Length of asystole prior to perfusion of coronary arteries, mins.*	*Remarks*
54	No	½	Yes	41	
55	No	2	Yes	25	
56	No	2	Yes	30	
57	Yes	3	Yes	30	Ventricular fibrillation stopped with 1 electric shock
58	Yes	3	Yes	48	Ventricular fibrillation stopped with potassium citrate
60	Yes	3	Yes	30	Animal sacrificed. Ventricular fibrillation stopped with potassium citrate
61	Yes	2	Yes	45	Animal sacrificed. Ventricular fibrillation stopped with potassium citrate
62	No	1	Yes	Total of 125 min. on extracorporeal circulation	Potassium asystole induced 6 times and cardiac action resumed each time. Animal sacrificed

All animals in this Table had 10 c.c. of 10 per cent sodium lactate injected into the proximal aorta during the process of resuscitation.

rhythm returned within 3 minutes without perfusion of the coronary arteries or any other resuscitative measures (Table I). These animals' hearts also were given a period of 1 to 2 minutes of coronary perfusion and then asystole was produced with potassium citrate in 5 per cent glucose. These also are included in both groups.

In a series of 5 acute experiments (dogs 62 through 66), the effects of insulin and glucose, either alone or in combination as a diluent for potassium citrate, were investigated (Table IV). In all animals with normal blood sugars, insulin plus potassium or these two in combination with glucose gave prompt and sustained asystoles.

The concentration of potassium in the systemic blood serum was measured in 4 cases (Table II). In these experiments the coronary blood during the cordial resuscitation was returned to the oxygenator, and recirculated, instead of being discarded. The only consistent change seen in the serum potassium concentration was immediately after induction of cardiac arrest by injection of potassium. After cardiac resuscitation the serum potassium concentration was higher than the initial measurement in 1 case.

In all, 23 consecutive animals (dogs 36 through 58) were subjected to potassium asystole and right ventriculotomy, with long term survival as the objective. The period of asystole varied from 14 to 70 minutes. Eight of these animals died. In 7 of the animals death occurred after a regular rhythm had returned. The cause of death appeared to be an ineffective ventricular contraction with resulting cardiac dilatation and death.

In the last 5 animals of this series (dogs 54 through 58) and 3 acute subsequent experiments (dogs 60, 61, and 62) sodium lactate was used in resuscitation of the heart (Table III). An effective regular ventricular contraction was established in all 8 animals. In 5 of these (dogs 57, 58, 60, 61, and 62) ventricular fibrillation occurred, but on breaking this abnormal rhythm either with electrical shock or potassium citrate a regular effective rhythm ensued.

The question of whether or not any strongly alkaline solution would do as well as sodium lactate was investigated in 2 animals (dogs 63 and 64). Ten per cent sodium bicarbonate solution was used instead of the sodium lactate. In these 2 cases the recovery period before establishment of ventricular contractions was longer than with sodium lactate, and cardiac action was ineffective.

DISCUSSION

The pioneer work describing the effect of various cations on cardiac rate and rhythm was reported by Ringer (9, 10, 11) in 1882. More pertinent to this discussion, Hooker, in 1929, used potassium chloride to stop ventricular fibrillation. He resuscitated these hearts using calcium chloride and adrenalin. Neither of these observers indicated the site or mode of potassium's action.

The experimental observations presented in this article are based entirely upon the minimal percentage of potassium (2.5 per cent) capable of producing prolonged cardiac asystole. The cardioplegic action of potassium is produced by prolonging the absolute refractory period of cardiac muscle. This prolongation by potassium can be potentiated for protracted periods by glucose. It seems fair to assume from this and work by others that: (1) the potassium is linked in some fashion with glucose to give this prolonged action, and (2) its site of action is extracellular.

Fenn postulated that potassium linked with phosphate ion to form a hexose phosphate when glucose, in association with insulin, was deposited as glycogen in the rats' liver. Such a linkage could be the means of glucose's potentiation of potassium asystole. Whether such a combination could give slow release of potassium with prolongation of the cardiac refractory period is unknown. Howell (5) showed a direct relationship between the heart's responsiveness to acetylcholine and serum potassium level. If the potassium asystole obtained is a profound acetylcholine effect, it is difficult to correlate with the dependency of prolonged asystole upon the presence of exogenous glucose or insulin in combination with potassium. The effect of insulin in combination with potassium in prolonging asystole suggests the linking of potassium with endogenous glucose. Insulin acts in this situation as a catalyst to secure the potassium-glucose linkage that reduces the myocardium to electrical neutrality.

It has been shown clinically and experimentally that elevation of the serum or extracellular potassium bears a direct relationship to electrocardiographic evidence of potassium intoxication of the heart. The converse or lowering of the extracellular potassium and raising the intracellular potassium reverts the signs of intoxication. Our observations show the inability of a 2½ per cent potassium citrate solution to produce asystole except for short periods (1 to 3 minutes), indicating the time necessary to balance osmotically the intracellular and extracellular concentration of potassium. This reduction of the high initial extracellular potassium concentration leads to an escape of the heart from asystole.

Thus, it appears that given a static flow situation, potassium in dilute concentrations

acts as a prolonged cardioplegic in an extracellular site when in intimate association with high concentrations of glucose. A similar prolonged cardioplegic response can be potentiated by insulin and potassium alone. Presumably, in this situation, insulin secures the rapid association of endogenous glucose and potassium. Such an association does not occur in the absence of this catalyst unless glucose is in concentrations above normal.

Preparations containing salts of lactic acid have been shown to be effective clinically as an aid in restoring effective cardiac rhythm in cases of atrioventricular heart block. Sodium lactate and Ringer's lactate have been used experimentally in cases of elective cardiac arrest. They apparently aid in restoration of a normal rhythm after elective cardiac arrest in hypothermic animals. In elective cardiac arrest of normothermic dogs with circulation supported by a pump oxygenator, the resuscitation of the heart is a major problem, as shown by the experimental work presented in this article. Eight animals died, and in 7 of these a regular rhythm was established before death resulted from ineffective ventricular contractions. Serum potassium levels in our study taken at the termination of aortic occlusion were not of a magnitude to account for this phenomenon. It appears from this observation that some mechanism other than the myocardial conduction system is responsible for death in these cases. In the 8 animals in which the myocardium was perfused with 10 per cent sodium lactate during the period of resuscitation, the return of regular effective ventricular contractions was prompt. This effect was not noted when sodium bicarbonate was used instead of sodium lactate. Bellet (6) has shown that sodium bicarbonate was not effective in protecting experimental animals from potassium toxicity, while sodium lactate was effective against toxicity. This fact suggests that neither the increased *p*H or the presence of the sodium ion is responsible for the beneficial effect of sodium lactate on cardiac action. Lactic acid is the important substance, and this is borne out by the experimental work of Evans, who has shown that the myocardium will preferentially metabolize lactic acid in the presence of adequate oxygenation. By increasing the concentration of lactic acid in the heart, the nutritional requirements of that organ can be met and its muscular contractions will become effective.

TABLE IV.—EFFECTS OF INSULIN AND GLUCOSE AS A DILUENT

Dog No.	*Blood sugar, mgm. per cent*	*Cardioplegic solution*	*c.c.*	*Cardioplegic action and amount of solution used in c.c.*
62	100	25% potassium citrate	2	Prolonged asystole 2 c.c.
		U-40 insulin	1	
		5% glucose in DW	17	
62		25% potassium citrate	2	Prolonged asystole
		U-40 insulin	1	
		Isotonic sodium chloride	17	
62		25% potassium citrate	2	Escape from asystole in ½ min.
		Isotonic sodium chloride	18	
63	160	25% potassium citrate	2	Prolonged asystole 5 c.c.
		U-40 insulin	1	
		5% glucose in DW	17	
64		25% potassium citrate	2	Prolonged asystole 4 c.c.
		U-40 insulin	1	
		Isotonic sodium chloride	17	
65		25% potassium citrate	2	Prolonged asystole 8 c.c.
		U-40 insulin	1	
		Isotonic sodium chloride	17	
66		25% potassium citrate	2	Prolonged asystole
		U-40 insulin	1	
		Isotonic sodium chloride	17	

CONCLUSIONS

1. Potassium citrate's cardioplegic action is potentiated by 5 per cent glucose. This potentiation is possibly due to a potassium-glucose bonding as a hexose phosphate.

2. Potassium and glucose in combination as a cardioplegic appear to act in an extracellular site in this static coronary vascular situation.

3. Insulin is an effective potentiator of potassium citrate asystole. Its action would seem to be as a catalyst to speed the potentiation of potassium action by either endogenous or exogenous glucose.

4. The serum potassium levels in elective potassium asystole are not of a magnitude to necessitate discarding the coronary sinus blood at the time of cardiac resuscitation.

5. Ten per cent sodium lactate is an effective cardiac resuscitating agent in cardiac standstill due to potassium intoxication.

6. Sodium lactate's action is not due to its alkalinity or sodium ion content but presumably to its nutritional attributes in a well oxygenated myocardium.

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THE FATE OF BLOOD IN THE PERITONEAL CAVITY

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MASSIVE INTRAPERITONEAL HEMORRHAGE is encountered not infrequently in the practice of obstetrics and gynecology. A laparotomy is performed, hemostasis is achieved, and frequently all or nearly all of the blood is removed from the peritoneal cavity. Should the removal of such blood be only sufficient to permit satisfactory exposure lest the patient be deprived possibly of an autotransfusion, as suggested by Curtis and Huffman, or should practically all of the blood be removed as recommended by Titus? This study was undertaken in an attempt to answer this and the following questions: What would be the fate of these erythrocytes in the peritoneal cavity if they were not removed? Would the patient benefit by leaving free blood in the peritoneal cavity at the time of surgery or would the risks involved outweigh the possible advantages? Are those laboratory tests which are frequently of value for detecting increased red cell destruction of any aid in diagnosing the presence of blood in the peritoneal cavity?

Recently in a preliminary study in humans, utilizing a method which allowed rather precise quantitation of the number of erythrocytes absorbed, it was observed that on the average two-thirds of the erythrocytes initially placed in the peritoneal cavity appeared in the intravascular compartment by the end of 1 week and that these erythrocytes then survived normally (4). The volume of blood introduced into the peritoneal cavity was small (50 to 100 milliliters) and this blood prior to being placed in the peritoneal cavity had been rendered incoagulable. Therefore the study did not determine the capacity of the peritoneum to absorb erythrocytes from large volumes of blood, nor did it determine the fate of erythrocytes in blood which was capable of clotting within the peritoneal cavity.

To measure precisely the number of red cells transferred from the peritoneal cavity to the intravascular compartment necessitates the labelling of the intraperitoneal erythrocyte. Ideally the label should be easily applied without damaging the red cell, it should remain bound to the erythrocyte as long as it remains intact, and when the red cell is destroyed the label must not be incorporated into another erythrocyte. Previous observations have indicated that radioactive chromium in the form of sodium chromate ($Na_2Cr^{51}O_4$) fulfills these criteria.

METHODS

The problem of the fate of erythrocytes in large volumes of blood in the peritoneal cavity was attacked in a number of ways. In 8 instances at the time of laparotomy performed for ruptured tubal pregnancy in patients with brisk bleeding into the peritoneal cavity, most of the liquid blood was aspirated into a 2 liter flask which contained 200 microcuries of $Na_2Cr^{51}O_4$ and 120 milliliters of acid citrate dextrose (ACD) solution. The flask was agitated frequently. Forty-five minutes to 1 hour later at the completion of the salpingectomy or salpingectomy plus hysterectomy the peritoneum was closed tightly with a purse-string suture around a rubber tube and through it a measured volume of the aspirated blood was replaced in the peritoneal cavity. The volumes introduced ranged from 475 to 1,150 milliliters and averaged 860 milliliters; the hematocrits of this blood ranged from 19 to 39 and averaged 25.

In 7 recently postpartum subjects who were otherwise normal, blood was drawn from the antecubital fossa into a blood bank

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bottle which contained 120 milliliters of ACD solution and 200 microcuries of $Na_2Cr^{51}O_4$ 1 to 2 hours before bilateral tubal ligation and partial resection were done because of great multiparity. After collection the bottle was occasionally agitated. Blood ranging in volume from 450 to 610 milliliters, and averaging 525 milliliters, was placed in the peritoneal cavity as in the previous group. The hematocrits of this blood ranged from 31 to 40 and averaged 36.

In these 2 groups of subjects clotting of the blood placed in the peritoneal cavity was inhibited by the ACD solution as well as by previous partial intraperitoneal clotting in several of the cases in which the blood was initially obtained from the peritoneal cavity. Therefore, to study the fate of intraperitoneal erythrocytes in blood which could readily clot, in 5 subjects blood was placed directly from a compatible donor into the peritoneal cavity at the time of bilateral tubal ligation and partial resection. Resident physicians of the same blood types as the recipients were selected as donors. Their blood was crossmatched using the indirect Coombs test as well as the standard technique with albumin. Several hours before the surgical procedure 50 milliliters of the donor's blood were tagged with 300 microcuries of $Na_2Cr^{51}O_4$ and then returned to the donor. At the time of closure of the peritoneum, blood was drawn directly from the donor through an 18 gauge coated needle into 50 milliliter silicone-coated syringes and was immediately injected into the peritoneal cavity. The total volume placed in the peritoneal cavity ranged from 450 to 500 milliliters and averaged 480 milliliters. The hematocrits of the donor blood varied from 44 to 49.

To determine the fate of intraperitoneal erythrocytes in clotted blood in 4 subjects, at the time of laparotomy for myomas or for sterilization, small blood clots containing the subject's labelled erythrocytes were placed in the peritoneal cavity. The erythrocytes in 50 milliliters of each subject's blood were labelled with 100 to 200 microcuries of $Na_2Cr^{51}O_4$ in a bottle containing 20 milliliters of ACD solution. At the start of laparotomy 4 milliliters of the blood were placed in each of 7 to 12 test tubes 13 millimeters in diameter to which had been added enough calcium chloride to overcome the anticoagulant action of the ACD solution. Just prior to closing the peritoneum the clots were "rimmed" with an applicator stick and dripped throughout the peritoneal cavity.

An aliquot of the labelled blood was saved in each case. The hematocrit was determined and 4 milliliters of the whole blood and 2 milliliters of the plasma plus 2 milliliters of water were placed in identical test tubes for measurement of erythrocyte radioactivity in a well-type scintillation counter. Venous blood was drawn at intervals of 1 to 4 days for 10 to 20 days after the intraperitoneal instillation, and in 10 of these subjects additional blood samples were obtained until the circulating erythrocyte radioactivity reached or closely approached zero. From the serial measurements of the radioactivity in the whole blood and plasma samples and from the hematocrit, the erythrocyte radioactivity per milliliter of blood was calculated. After the first 24 hours the circulating plasma radioactivity was negligible, all of the radioactivity being bound to the circulating erythrocytes. All measurements of radioactivity were corrected for physical decay of the isotope.

Five to 10 days after the intraperitoneal instillation of the labelled erythrocytes the plasma volume, and indirectly the approximate total circulating blood volume, was determined using Evans blue dye. The degree of absorption of intraperitoneal erythrocytes, expressed as per cent, was calculated from the following formula:

$$\text{Per cent absorbed} = \frac{\text{RBC activity per ml. of blood} \times \text{Blood volume}}{\text{Total intraperitoneal RBC activity}} \times 100$$

Serial measurements of the plasma bilirubin concentration were made in 13 subjects and the amount of urobilinogen excreted in the urine was measured in 10 subjects, the former by the method of Malloy and Evelyn

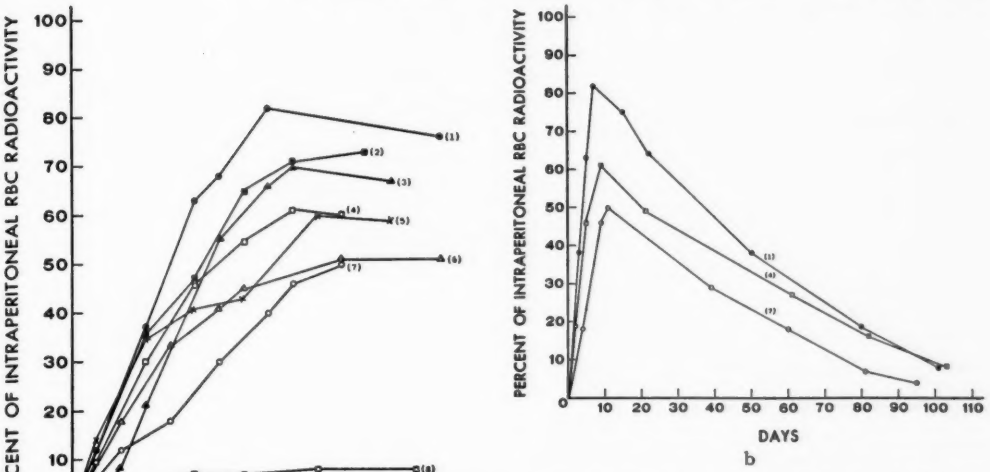

FIG. 1. a, Plotted are the circulating erythrocyte radioactivities, expressed as per cent of the initial intraperitoneal red cell radioactivity, which developed following aspirating, labelling, and replacing in the peritoneal cavity blood resulting from a ruptured tubal pregnancy with massive hemorrhage. b, Demonstrated is the duration of circulating erythrocyte radioactivity in 3 of the subjects in (a), indicating that the red cells absorbed from the peritoneal cavity survived normally.

and the latter by the method of Watson and associates. The patients were observed for clinical evidence of jaundice.

All urine was collected from 1 subject who received her own labelled erythrocytes initially obtained from the peritoneal cavity and from 1 who received labelled blood directly from a donor, and the daily urinary excretion of radioactive chromium was determined.

OBSERVATIONS

Blood replaced in peritoneal cavity. As shown in Figure 1a, in 7 of the 8 subjects with a ruptured ectopic pregnancy in whom blood was aspirated from the peritoneal cavity and then reintroduced after labelling, there was considerable transfer of labelled erythrocytes from the peritoneal cavity to the intravascular compartment. The maximum circulating erythrocyte radioactivity which resulted in each of these 7 ranged from 50 to 82 per cent and averaged 64 per cent of the amount introduced. The maximum was reached in 8 to 12 days.

To determine the life span of the absorbed red cells in 3 instances the circulating erythrocyte radioactivity was measured until it reached or closely approached zero and, as shown in Figure 1b, radioactivity was detected for a minimum of 95 days.

No clinical evidence of jaundice was observed in these 7 subjects. Serial serum bilirubin levels were determined in 4; the highest serum bilirubin concentration in each ranged from 0.5 to 1.3 milligrams per 100 milliliters. Daily urine urobilinogen excretion was measured in 3 and in each instance was less than 1.0 Ehrlich unit per 2 hours.

Reintroduction of blood into the peritoneal cavity was not followed by shoulder pain. The degree of abdominal distention which developed during the early postoperative period in these subjects seemed to be appreciably greater than usually seen after such an operation. The degree of absorption of labelled erythrocytes was not consistently related to either the patients' hematocrits during the immediate postoperative period or the volumes of blood introduced (Table I).

TABLE I.—INDIVIDUAL OBSERVATIONS FOLLOWING THE INTRODUCTION OF BLOOD INTO THE PERITONEAL CAVITY

Subject	*Intraperitoneal blood, ml.*	*Hematocrit, postop.*	*Absorbed RBC, per cent*	*Days until maximum*	*Maximum bilirubin, (mgm./100 ml.)*	*Shoulder pain*
I. Ruptured ectopic						
1	1070	35	82	8	1.0	0
2	970	28	73	12	1.3	0
3	1100	26	70	9	0.8	0
4	915	23	61	9	—	0
5	620	27	60	10	0.5	0
6	475	30	51	11	—	0
7	600	26	50	11	—	0
8	1150	29	8	—	2.1	0
II. ACD blood						
9	610	39	77	16	—	+
10	575	39	76	10	0.7	0
11	450	39	69	9	0.6	+
12	550	35	68	14	0.7	0
13	530	38	64	16	—	+
14	490	38	41	14	—	0
15	475	43	41	15	0.8	+
III. Donor blood						
16	500	39	60	7	—	0
17	450	38	52	8	0.8	+
18	475	40	46	8	0.7	+
19	500	36	30	16	0.5	0
20	475	42	20	8	0.7	+

I. — Blood initially obtained from the subject's peritoneal cavity.
II. — Blood drawn from the subject's vein.
III. — Blood without ACD solution obtained from a compatible donor.

In 1 of these subjects erythrocyte transfer from the peritoneal cavity to the intravascular compartment accounted for less than 10 per cent of the cells initially placed in the peritoneal cavity and finally the remaining blood had to be removed:

L. D. P. was apparently normal until she bled rapidly and massively into the peritoneal cavity from a ruptured tubal pregnancy. At the time of laparotomy no other intra-abdominal abnormality was noted; there was no evidence of either recent or remote peritonitis. Following tubal resection 1,150 milliliters of blood were replaced in the peritoneal cavity.

On the first postoperative day there was bulging of the flanks and shifting dullness within the abdomen. At this time bowel sounds were present and patient expelled flatus. Her temperature rose briefly to a maximum of 100 degrees 48 hours after surgery. The serum bilirubin reached 2.1 milligrams per 100 milliliters.

Four days after surgery circulating erythrocyte radioactivity accounted for only 7 per cent of the erythrocyte radioactivity placed in the peritoneal cavity. Culdocentesis yielded thick blood with a hematocrit of 75; a smear of this blood revealed the structure of most of the erythrocytes to be normal. This material contained considerable radioactivity.

A further rise in circulating erythrocyte radioactivity did not occur. The patient remained asymptomatic and afebrile. On the eleventh postoperative day another culdocentesis was performed. The bloody material obtained was again very thick. The structure of the erythrocytes was considerably distorted and numerous red cell "ghosts" were present.

Four days later, the fifteenth postoperative day, her temperature rose to 102 degrees and she complained of lower abdominal pain. At this time the peripheral blood again contained only 8 per cent of the erythrocyte radioactivity originally placed in the peritoneal cavity. A colpotomy was done and about 500 milliliters of thick bloody material were obtained which when cultured yielded Escherichia coli. The patient promptly recovered.

Citrated blood from a peripheral vein. In the 7 apparently normal subjects in whom their own blood was drawn from a peripheral vein into $Na_2Cr^{51}O_4$-ACD solution and then placed in the peritoneal cavity there was considerable transfer of erythrocytes to the intravascular compartment. The maximum circulating erythrocyte radioactivity in each ranged from 41 to 77 per cent and averaged 62 per cent of the initial intraperitoneal erythrocyte radioactivity; these levels were reached in 8 to 14 days (Fig. 2a). There was no apparent correlation between the subjects' hematocrits and the amount of red cell absorption (Table I).

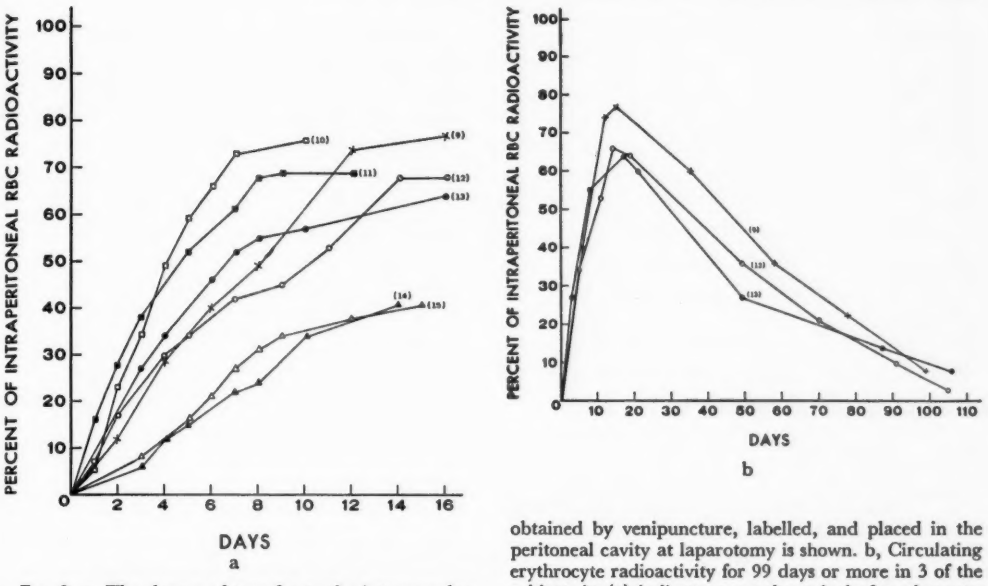

FIG. 2. a, The degree of transfer to the intravascular compartment of the subjects' erythrocytes which were obtained by venipuncture, labelled, and placed in the peritoneal cavity at laparotomy is shown. b, Circulating erythrocyte radioactivity for 99 days or more in 3 of the subjects in (a) indicates normal survival of erythrocytes absorbed from the peritoneal cavity.

In 3 instances the duration of circulating erythrocyte radioactivity was determined and, as shown in Figure 2b, it was detected for a minimum of 99 days after placing blood in the peritoneal cavity.

The operation was carried out by using spinal anesthesia. Shoulder pain developed within 10 minutes to 2 hours after the intraperitoneal instillation of the citrated blood in 4 of 7 subjects and disappeared in 16 to 48 hours. During the early postoperative period abdominal tenderness and intestinal distention seemed more marked than usually seen after this operation; gastrointestinal intubation was not necessary however.

There was no clinical evidence of jaundice following the intraperitoneal instillation of blood. The highest serum bilirubin level noted in 4 of these subjects ranged from 0.6 to 0.8 milligram per 100 milliliters. Daily urine urobilinogen excretion measured in 4 was less than 1.0 Ehrlich unit per 2 hours.

Compatible donor blood directly into the peritoneal cavity. In the 5 subjects who received intraperitoneally labelled compatible erythrocytes in blood directly from suitable donors, rather than their own citrated blood, the maximum circulating erythrocyte radioactivity accounted for 20 to 60 per cent and averaged 42 per cent of the initial intraperitoneal erythrocyte radioactivity (Fig. 3). Maximum absorption was reached in 7 to 16 days. Again there was no apparent correlation between the subjects' hematocrits and red cell absorption (Table I).

The duration of circulating erythrocyte radioactivity was measured in 4. It was considerably shortened in 2 (subjects 16 and 17), averaging only 40 days, but in the other 2 (subjects 18 and 19) it was normal. Studies in the 2 subjects with shortened survivals, including a search for abnormal hemoglobin by filter paper electrophoresis, revealed no hematologic abnormality. Furthermore, in both instances the donor's cells survived in him for at least 100 days.

No clinical evidence of jaundice followed the intraperitoneal instillation of blood; maximum serum bilirubin concentration ranged from 0.5 to 0.8 milligram per 100 milliliters. Daily urine urobilinogen excretion was less than 1.0 Ehrlich unit per 2 hours.

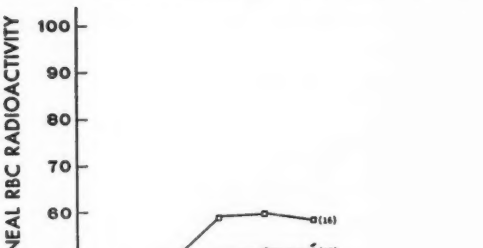

FIG. 3. Demonstrated is the amount of transfer of erythrocytes from the peritoneal cavity to the intravascular compartment following the introduction of donor blood without ACD solution into the peritoneal cavity.

Tubal ligation and partial resection were performed by using spinal anesthesia. In 3 out of 5 instances shoulder pain developed 10 minutes to 2 hours after the intraperitoneal instillation of blood and lasted for 24 to 48 hours. In all but 1 there was more generalized abdominal tenderness and abdominal distention than usually seen after this operation. In 1 the degree of ileus necessitated gastrointestinal intubation and constant suction.

Labelled erythrocytes in blood clots. As shown in Figure 3, the percentage of erythrocytes transferred to the intravascular compartment after placing numerous small blood clots in the peritoneal cavity usually was much less than when the blood was added in the liquid state. The maximum circulating erythrocyte radioactivity accounted for only 15 to 29 per cent and an average of 22 per cent of the labelled erythrocytes placed in the peritoneal cavity. There was no evidence that the introduction of these relatively small blood clots into the peritoneal cavity was deleterious to the patient.

Urinary excretion of Cr^{51}. In subject No. 2 the total radioactivity placed in the peritoneal cavity in blood originally obtained from the peritoneal cavity was 17,400,000 counts per minute (CPM); 13,600,000 CPM, or 78 per cent of the total radioactivity, were bound to the red cell fraction. During the first 24 hours after placing the labelled blood in the peritoneal cavity 4,050,000 CPM appeared in the urine, slightly more than the 3,800,000 CPM which were not bound to the erythrocytes. During the second 24 hours the urine radioactivity was 2.8 per cent of the radioactivity bound to the erythrocytes placed intraperitoneally. Urinary Cr^{51} excretion slowly fell during the next week to reach 1.1 per cent of the initial intraperitoneal erythrocyte radioactivity on the ninth postoperative day. Circulating erythrocyte radioactivity reached a maximum of 73 per cent on the twelfth day; the amount of radioactivity which had appeared in the urine plus that in the circulating erythrocytes accounted for 91 per cent of the radioactivity originally placed in the peritoneal cavity.

In subject No. 18 labelled erythrocytes were provided by a compatible donor. All of the radioactivity in the donor blood was bound to the erythrocytes. Excretion of Cr^{51} comparable to that in this subject did not occur during the first 24 hours after the introduction of labelled blood into the peritoneal cavity, presumably because all the intraperitoneal radioactivity was bound to the red cells. Instead, the urine radioactivity rose progressively to reach 6 per cent of the initial intraperitoneal radioactivity on the fifth postoperative day. It then fell to 2.8 per cent on the eighth day, the last day of measurement of urinary Cr^{51} excretion. At this time the amount of radioactivity excreted in the urine plus that in the circulating blood accounted for 74 per cent of the amount placed in the peritoneal cavity.

DISCUSSION

These studies indicate that the introduction of a relatively large volume of the sub-

ject's own blood mixed with ACD solution into the peritoneal cavity is usually followed by the transfer of about two-thirds of the red cells from the peritoneal cavity to the intravascular compartment where the absorbed cells survive normally. However, when whole blood from presumably compatible donors is placed directly into the peritoneal cavity without the addition of ACD solution, the number of erythrocytes subsequently appearing in the circulating blood may be appreciably less.

In spite of the use of the indirect Coombs test as well as standard cross-matched procedures, an explanation which must be considered for the rather marked increase in the rate of disappearance of circulating erythrocyte radioactivity in 2 of the subjects who received donor blood is that the donor's red cells may have been incompatible with the recipient's blood. In any event, since both the recipients and the donors were hematologically normal, the shortened life spans observed in these 2 subjects supply further proof that erythrocyte radioactivity which appeared in the blood stream resulted from the actual transfer of labelled erythrocytes from the peritoneal cavity rather than from intraperitoneal erythrocyte destruction, followed by just the transfer of radioactive chromium to the erythrocytes already in the intravascular compartment. If the latter were the mechanism by which circulating erythrocyte radioactivity developed, the radioactivity should have persisted for more than 90 days, rather than about 40 days as observed in these 2 instances.

Although the volumes of blood replaced in the peritoneal cavities of subjects with ruptured tubal pregnancies were frequently quite large, averaging 860 milliliters, the red cell concentration was appreciably reduced; the hematocrits were as low as 19 and averaged only 25. These rather low hematocrits undoubtedly resulted from the combination of previous clotting of some of the blood within the peritoneal cavity with subsequent dilution of the liquid blood by serum, to some extent from the lowered

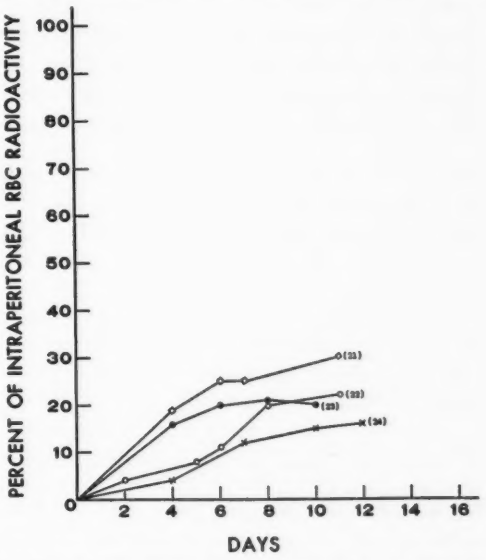

FIG. 4. The degree of absorption of erythrocytes is shown following the introduction of numerous small blood clots containing labelled erythrocytes into the peritoneal cavity.

hematocrits of the subjects' circulating blood, and to a lesser degree from dilution of the aspirated blood by the ACD solution.

Actually the total amount of hemoglobin in red cells placed in the peritoneal cavity was quite similar in all 3 groups, ranging from 63 to 71 grams. The amounts of hemoglobin in erythrocytes transferred to the intravascular compartment from the peritoneal cavity at the end of an average interval of 10 days, excluding subject No. 8 from group I, amounted to only 41 grams, 39 grams, and 29 grams in groups I, II, and III respectively. In cases of iron deficiency or acute hemorrhage the usual minimal response to iron therapy is an increase in hemoglobin concentration of 1.0 gram per week. Therefore the female patient with a blood volume of 4,000 milliliters who is supplied with iron can be counted upon to make a minimum of about 60 grams of hemoglobin during a 10 day period, an appreciably greater amount than usually was absorbed from the peritoneal cavity during the same period of time by these subjects.

On the other hand, though erythrocyte absorption was incomplete, all or nearly all of the iron in the intraperitoneal blood ultimately would become available for hemoglobin synthesis, but the loss of this iron as the result of removing and discarding blood found free in the peritoneal cavity need not be considered important since replacement iron can be readily given as iron salts orally, saccharated iron oxide intravenously, or iron-dextran intramuscularly.

Measurements of the serum bilirubin concentration and urobilinogen excreted in the urine proved of little value for detecting the presence of free blood in the peritoneal cavity; the serum bilirubin level was above 1.0 milligram per 100 milliliters in only 2 out of 13 subjects, and the urinary excretion of urobilinogen was not abnormal in any of 10 subjects.

The presence of a considerable volume of blood in the peritoneal cavity during the postoperative period not infrequently seemed to be disadvantageous to these patients. The most striking instance was noted in subject No. 8 in whom ultimately the intraperitoneal blood localized in the pelvis and became infected, necessitating drainage through the cul-de-sac. In others the febrile response and the degree of ileus during the early postoperative period appeared more marked than usually seen following these operations. No irreversible harm to any of the subjects was apparent however. Some of these untoward reactions may have resulted from the manipulations necessary for collecting, labelling, and introducing the blood into the peritoneal cavity, although every attempt was made to maintain asepsis and antibiotics were given prophylactically for 5 to 7 days.

The exact mechanism by which shoulder pain is produced as the result of blood in the peritoneal cavity was not determined. Replacement of the blood in the peritoneal cavity under general anesthesia in cases of ruptured tubal pregnancy was not followed by shoulder pain. However 4 out of 7 subjects who received their own citrated blood intraperitoneally at the time of surgery under spinal anesthesia developed shoulder pain, as did 3 out of 5 who similarly received compatible donor blood without an anticoagulant. It is interesting that the incidence of shoulder pain in these latter 2 groups was 7 out of 12, or 59 per cent, and in cases of intra-abdominal hemorrhage following trauma Altemeier and associates noted it to be present in 17 out of 30, or 57 per cent.

The incompleteness and especially the slow rate of red cell absorption observed in these patients indicate that the intraperitoneal route for blood transfusion therapy is impractical if it is assumed that the patient who receives blood by transabdominal injection transfers erythrocytes from the peritoneal cavity to the intravascular compartment in an amount and at a rate comparable to those observed in these subjects during the postoperative period.

SUMMARY AND CONCLUSIONS

When a relatively large volume of blood, obtained either from the peritoneal cavity following rupture of an ectopic pregnancy or simply drawn from the subject's vein, is mixed with ACD solution and placed in the peritoneal cavity during laparotomy, on the average, two-thirds of the intraperitoneal erythrocytes are subsequently transferred to the intravascular compartment. The period of erythrocyte absorption is prolonged, demonstrable absorption being present for 7 to 16 days after placing such blood in the peritoneal cavity. Following their transfer to the blood stream the erythrocytes survive normally.

When a comparable number of erythrocytes in blood from presumably compatible normal donors but without added ACD solution is similarly placed in the peritoneal cavity, the apparent absorption is reduced.

Relatively slight effect on the level of circulating hemoglobin from actual transfer of hemoglobin in erythrocytes from the peritoneal cavity to the intravascular compartment can be anticipated from erythro-

cyte absorption. Although the volumes of blood placed in the peritoneal cavity frequently were quite large, the amount of hemoglobin transferred to the intravascular compartment compared to the subject's total hemoglobin mass was actually quite small. The administration of iron can be counted upon to result usually in hemoglobin production considerably in excess of the amount in erythrocytes transferred to the blood stream during the same period of time.

Measurements of the serum bilirubin concentration or urine urobilinogen excretion usually are of little value for detecting the presence of blood free in the peritoneal cavity.

While the presence of a large volume of blood in the peritoneal cavity results in no apparent irreversible harm, its presence may be disadvantageous to the patient for often increased postoperative morbidity results.

It is recommended that in cases of extensive intraperitoneal hemorrhage the blood be removed at the time of laparotomy and that iron be given to replace the amount lost in the discarded hemoglobin.

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SADDLE BLOCK ANESTHESIA IN BREECH DELIVERY

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THE GOLDEN PINNACLE in obstetric anesthesia of complete relief from the pain and discomfort of labor, without harmful effects to mother or infant, has not yet been achieved. In this regard it is realized that to date no one type of anesthesia represents a panacea, and each case must be judged on the clinical factors that are present.

The safety of saddle block anesthesia in obstetrics has been amply proved in the case of both mother and infant by Adriani and Parmley. In 1950, it was estimated that saddle block was used in approximately one-fourth of the births in the maternity centers on the West Coast, and in Springfield, Massachusetts, saddle block anesthesia was used in 10,000 consecutive deliveries without a single maternal mortality.

The series now presented deals with the use of saddle block anesthesia in breech presentations. Manson was the first to report the administration of caudal anesthesia in breech delivery, and because of the good results achieved he later reported on a series of breech deliveries using saddle block anesthesia. The excellent results he obtained, and the fact that there has, to our knowledge, appeared no other series, has led us to conduct the present study, not forgetting the general condemnation of saddle block anesthesia for breech delivery elsewhere. The main question to be answered is, what reason—if any—is there why saddle block anesthesia should be more dangerous in breech delivery than in vertex presentation? We have been told that this is because the cervix is tight and unrelaxed, and that the infant's head is often difficult to deliver as a result. Further, we have been told that saddle block anesthesia often necessitates complete breech extraction in the face of incomplete uterine relaxation. Our feeling is that the debate is not between saddle block anesthesia and other methods in breech delivery but, rather, between the relative safety of assisted breech deliveries (partial breech extraction) and complete breech extraction. We would certainly agree from the outset that complete breech extraction is an unwise procedure under saddle block anesthesia. Complete breech extraction should not be performed routinely but only on the basis of strict indication and necessity. We say this for the following reasons: (1) Complete uterine relaxation, which is necessary for complete breech extraction, is achieved only by profound, deep ether anesthesia or the use of chloroform. (2) Even under these circumstances the lower extremities of the infant may be injured. (3) The type of anesthesia mentioned not only causes uterine relaxation for the delivery, but resides to cause uterine atony which is a major factor in obstetric deaths from hemorrhage. (4) It is unnecessary to add that this profound anesthesia also causes fetal depression and anoxia.

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METHODS

Our study is taken from the Obstetrical Department at Jefferson Davis City-County Hospital, which cares for the indigent sick who are managed by the House Staff. Approximately one-third of all patients delivered are unregistered and have received no prenatal care. From July 1, 1952 to May 1, 1956, there were 13,389 deliveries, 486 (3.6 per cent) of which were breech, and the infants weighed 1,000 grams or over. Of the infants delivered (1,000 gm. and over) 169 were delivered under saddle block anesthesia by the method of assisted breech extraction (partial breech extraction). A standard program of analgesia was in operation with demerol, seconal, and

scopolamine. During the past year chlorpromazine (thorazine) has been added to the regimen to potentiate these drugs, thus eliminating barbiturates, and permitting a reduction in the total dosage of demerol.

The following precepts were laid down for the type and timing of the saddle block in these cases: (1) A standard type procedure for the administration of saddle block was used, that is, the block was given in the third and fourth lumbar interspace, with the patient sitting up for a period of precisely 30 seconds. (2) The agent used was 4 milligrams of pontocaine in 2 cubic centimeters of 10 per cent dextrose. (3) In primigravidas the saddle block was given at the time the presenting part was on the perineum and visible without spreading the labia. (4) In multiparas, particularly those with rapid progress in labor, the saddle block was given according to dilatation, station, and progress in labor. In no instance was the saddle block given unless the cervix was dilated at least 8 centimeters, and the presenting part at +2 to +3 station. In order to have a comparable control group of patients, the type of delivery anesthesia was left to the discretion of the delivering resident, and no restrictions were placed upon the type of patient, whether complicated or not, who was to be delivered under saddle block, with the exception that the saddle block was not used if complete breech extraction was anticipated or indicated. In these circumstances deep ether anesthesia is our method of choice. In the rare instance in which a mistake of judgment has been made, particularly in multiparas, and the saddle block is given too early, we simply allow the patient to recover from the anesthesia and her contractions to resume, in which case the perineal effect of the saddle block lasts for a greater period of time and is usually adequate for the episiotomy repair.

RESULTS

In 169 breech deliveries under saddle block anesthesia the sampling groups, according to birth weights, may be seen in Figure 1 to compare favorably with the same groups under other types of anesthesia. It was not the House Staff's intention to deliver any of the patients under trimar or local anesthesia, or without any anesthesia, but these patients are a special group with whom one has to contend in any large charity hospital. They are patients in whom proper timing of the saddle block could not be anticipated, imminent delivery making it necessary to use some other type of anesthesia, or no anesthesia at all. Saddle block anesthesia in our hands has given a much more significant relief of pain during delivery, as well as more control over the delivery itself, than have trimar, pudendal, or local perineal anesthesia.

FIG. 1. Types of anesthesia and deaths in relation to birth weight groups.

In both groups (those with saddle block and those receiving various other types of anesthesia) 35 per cent of the infants were either one or both of a twin delivery. Infants delivered as breech, after version and extraction, were not considered in this series. In twins, under saddle block anesthesia, when the second twin presented as a breech, membranes were ruptured and the delivery carried out as an assisted breech extraction. It is of interest to note that of the 5 stillborn infants in the term saddle block group, not one of these was an intrapartum death, all being antepartum.

Figures 2 and 3 represent: (1) the percentage of perinatal mortality, that is, including all deaths of infants weighing 1,000 grams and over; and, (2) for comparison, the neonatal mortality in infants of 1,000 grams and over, which we believe is a more accurate representation of deaths caused by anesthetic agents.

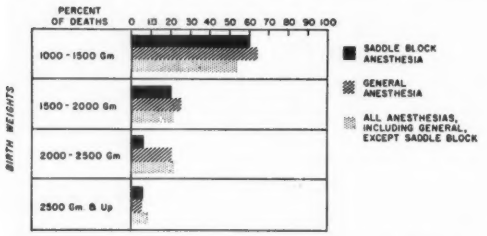
PERCENT OF DEATHS
0 10 20 30 40 50 60 70 80 90 100
1000 - 1500 Gm
1500 - 2000 Gm
2000 - 2500 Gm
2500 Gm & Up
BIRTH WEIGHTS
SADDLE BLOCK ANESTHESIA
GENERAL ANESTHESIA
ALL ANESTHESIAS, INCLUDING GENERAL, EXCEPT SADDLE BLOCK

FIG. 2. Per cent perinatal mortality in breech deliveries from July 1, 1952 through April 30, 1956 by birth weight and according to types of delivery anesthesia.

Perinatal mortality (Fig. 2). These data cover that period from July 1, 1952 to May 1, 1956 and represent a total of 486 infants delivered by breech extraction. The anesthesia was divided into three groups: (1) saddle block, (2) general anesthesia, and (3) all anesthetics including general, but excluding saddle block.

Group I (2,500 gm. and over).—There were 101 births under saddle block and 6 deaths (none intrapartum), a 6 per cent mortality. Under general anesthesia there were 90 deliveries and 6 deaths, or a 5.5 per cent mortality. In the "all anesthetics" group there were 177 deliveries with 14 deaths, a mortality of 8 per cent.

Group II (2,000 to 2,500 gm.).—Under saddle block there were 2 deaths in 30 deliveries, or a mortality of 6.7 per cent; under general anesthesia there were 4 deaths in 21 deliveries, or a mortality of 20 per cent; and in the "all anesthetics" group, there were 50 deliveries and 11 deaths, a mortality of 22 per cent.

Group III (1,500 to 2,000 gm.).—There were 21 infants under saddle block anesthesia, with 4 deaths (none intrapartum), or a mortality of 20 per cent; 16 infants were delivered under general anesthesia, with 4 deaths, or a mortality of 25 per cent; and in the "all anesthetics" group there were 29 infants with 6 deaths, a mortality of 21 per cent.

Group IV (1,000 to 1,500 gm.).—There were 17 infants delivered under saddle block, with 10 deaths (none intrapartum), which represents a 60 per cent mortality. Under general anesthesia there were 14 infants and 9 deaths, making a 64 per cent mortality, and in "all anesthetics" there were 61 infants, with 31 deaths, or a mortality of 51 per cent.

Neonatal mortality (excluding intrapartum and antepartum deaths) (Fig. 3). Group I (2,500 gm. and over).—There was 1 death under saddle block anesthesia in this group of 96 deliveries, or a mortality of 1 per cent. Under general anesthesia there were 2 deaths in 87 infants, or a mortality of 2 per cent; and in the "all anesthetics" group there were 6 deaths in 169 infants, or a mortality of 3.5 per cent.

Group II (2,000 to 2,500 gm.).—In the saddle block group there were 29 infants with 1 death, or a mortality of 3 per cent. Under general anesthesia there were 4 deaths in 21 infants, or a mortality of 20 per cent; and in the "all anesthetics" group there were 9 deaths in 49 infants, or a 19 per cent mortality.

Group III (1,500 to 2,000 gm.).—Under saddle block there was a 15 per cent mortality with 3 deaths in 20 infants; under general there was a 25 per cent mortality with 4 deaths in 16 infants; and in "all anesthetics" there was a 15 per cent mortality with 4 deaths in 27 infants.

Group IV (1,000 to 1,500 gm.).—In the saddle block group there were 16 infants and 9 deaths, or a 56 per cent mortality; in the general group there were 13 infants with 8 deaths, or a 60 per cent mortality, and in the "all anesthetics" group there were 57 infants, with 28 deaths, or 50 per cent mortality.

Résumé of deaths of infants born of those patients receiving saddle block anesthesia (excluding those infants weighing 1,500 gm. and less). Group I (2,500 gm. and over).—In this group, 5 of the 6 deaths were of stillborn infants, fetal heart tones having ceased prior to administration of saddle block. None of the 5 was a difficult assisted breech extraction, and we believe that anesthesia contributed in no way to the fetal death which occurred before anesthesia was given. The

sixth death in this group related to the infant of a 22 year old, white, unregistered, gravida 2 para 1, at term, who was admitted in active labor with approximately 8 centimeters of cervical dilatation. She achieved complete dilatation in 1 hour and 45 minutes following admission. On admission her membranes had ruptured spontaneously. Fetal heart tones were heard and were of good quality. Her blood pressure was 166/108, temperature 99.6, and there was a trace of albumin in her urine. No edema was present. Her analgesia consisted of 100 milligrams of demerol and 0.4 milligram of scopolamine. Saddle block anesthesia was given at full dilatation and +2 station, and her blood pressure dropped to 130/95. An uncomplicated, assisted breech delivery was performed, using Piper forceps to the aftercoming head, over a right mediolateral episiotomy. At birth the infant was in poor condition and required intratracheal aspiration and resuscitation. The infant lived for 30 hours. Autopsy revealed deep anoxia, and aspiration of meconium into the respiratory tract. The time between the saddle block anesthesia being administered and the delivery of the infant was 40 minutes, which time also represented the duration of her second stage of labor. During her postpartum course the patient's blood pressure remained at normotensive levels without treatment. This infant presented as a double-footling breech and one wonders whether or not unrecognized cord compression may have been present. We do not believe that the anesthesia contributed to the infant's death, since delivery was neither difficult nor delayed. The postmortem diagnosis agreed with the clinical impression, namely, death due to acute anoxia, and aspiration of meconium into the respiratory tract.

Group II (2,000 to 2,500 gm.).—Only 2 deaths occurred in this group, one a stillborn infant, no fetal heart tones having been heard during the latter part of her labor prior to the administration of her anesthesia.

In the second case, a 21 year old, colored, gravida 3 para 2, with twins was admitted

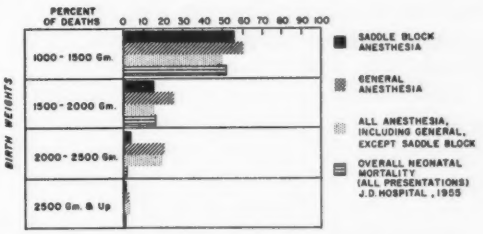
PERCENT OF DEATHS
0 10 20 30 40 50 60 70 80 90 100
BIRTH WEIGHTS
1000 - 1500 Gm.
1500 - 2000 Gm.
2000 - 2500 Gm.
2500 Gm. & Up
SADDLE BLOCK ANESTHESIA
GENERAL ANESTHESIA
ALL ANESTHESIA, INCLUDING GENERAL, EXCEPT SADDLE BLOCK
OVERALL NEONATAL MORTALITY (ALL PRESENTATIONS) J.D. HOSPITAL, 1955

FIG. 3. Per cent neonatal mortality in breech deliveries from July 1, 1952 through April 30, 1956 by birth weight and according to types of delivery anesthesia.

early in labor at 36 weeks' gestation. The patient received minimal analgesic dosages because of the anticipated small size of her infants. After an 8 hour first stage of labor, twin "A" presented as a complete breech at the introitus. Saddle block anesthesia was given and the patient was immediately put up for delivery. Vaginal examination revealed an occult prolapse of the cord with very faint pulsations. An immediate, assisted breech extraction was done with Piper forceps to the aftercoming head, but it was apparently too late, as the infant was limp at delivery and the heart beat was very slow and irregular. Approximately 15 cubic centimeters of amniotic fluid were aspirated from the trachea, an airway was established, and 100 per cent oxygen was given. There was no improvement, however, and the infant died soon after delivery.

Group III (1,500 to 2,000 gm.).—There were 4 deaths in this group, the first being a stillborn infant, the fetal heart tones having ceased prior to the administration of anesthesia.

In the second case, a 33 year old, white, gravida 3 para 2 was admitted in premature labor. She also had an acute pyelonephritis with a temperature of 101.4 degrees and urine loaded with pus cells. Catheterized urine was obtained for culture and sensitivity, and the patient was meanwhile placed on gantrisin. She had an uneventful 7 hour labor and delivery over a right mediolateral episiotomy. The infant was in good condition at the time of delivery and cried spontaneously but died 9 hours after delivery.

Autopsy revealed what the Pediatric Department had suspected—reabsorption atelectasis with hyaline membrane disease.

In the third case, a 33 year old, colored, gravida 5 para 4, unregistered patient was admitted in premature labor. Her blood pressure was 120/80, temperature 98.6, serology negative, Rh positive. After 5 hours of labor a normal premature infant was delivered as an assisted breech extraction over a right mediolateral episiotomy. The infant cried spontaneously and did well until it died suddenly 11½ hours following delivery. Autopsy revealed petechial hemorrhages throughout heart and lungs.

In the fourth case, a 36 year old, colored, unregistered, gravida 8 para 6 was admitted in premature labor. After 3 hour labor she delivered twins (twin "B" being a breech) without difficulty, under saddle block anesthesia. The membranes were ruptured at the time of delivery and the amniotic fluid was very cloudy, with a slightly green tinge. The infant was in poor condition at birth and required intratracheal aspiration. It lived 41 hours and the pathologic findings were focal hemorrhages of the epicardium and lungs.

SUMMARY AND CONCLUSIONS

1. Although our series is not large, we believe that saddle block anesthesia is a safe and effective anesthetic in breech delivery. Its safety concerns both mother and infant. It offers a more complete type of relief to the mother, and the infant rarely requires resuscitation, which is so often necessary when general anesthesia is used.

2. No maternal complication in this series is attributable to the use of saddle block anesthesia.

3. Saddle block anesthesia could not, in our opinion, be held responsible for any infant deaths which occurred in this study.

4. Saddle block should be used only in conjunction with assisted breech delivery (partial breech extraction) which in our experience is the safest method of breech delivery, regardless of the anesthesia used.

5. When deep ether is required for complete breech extraction it is not contraindicated as an addition to any previous saddle block anesthesia that may have been given, as a smaller amount of ether may be used and the anesthesia discontinued immediately after delivery since the saddle block will be adequate for episiotomy repair.

6. In infants weighing over 2,000 grams the highest salvage rate was obtained under saddle block anesthesia.

7. It is realized that there are other safe methods of obstetric anesthesia in breech delivery, for example, a combination of pudendal block and cyclopropane, but we believe that saddle block anesthesia is certainly equal to any known type of anesthesia for assisted breech delivery and, for this reason, does not deserve the condemnation it has received.

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EDITORIALS

CARCINOMA AND ARTERIAL DISEASE

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THE RELATIONSHIP between carcinoma and an increased incidence in venous thrombosis has been well documented. This phenomenon has been particularly apparent as it relates to carcinoma of the pancreas. However, there has been little or no comment made concerning the possible association between the simultaneous presence of carcinoma and symptoms of arterial insufficiency of the lower extremity.

At a recent local clinical meeting, a case in point was presented. Briefly, the patient was a 63 year old white male complaining of pain in the right small toe of 5 weeks' duration. The patient's left leg had been amputated about 15 months previously because of advanced arteriosclerotic symptoms. The pain gradually had increased and involved the third and fourth toes as well. An aortogram revealed a block of the right common iliac artery. An endarterectomy was performed. The clinical result of this procedure was excellent. Five months later, the patient returned because of pain in the left shoulder and a cough of 3 weeks' duration. X-ray examination of the chest revealed a rounded homogeneous mass in the right lung. Review of previous films of the chest taken 6 months and 2 years before showed the same, but somewhat smaller mass. The patient was given palliative radiation treatment for the lung carcinoma and he died about 8 months later. In the discussion which followed this case presentation, the panel did not mention any possibility of correlation between the two disease entities.

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A personal experience has led me to believe that such an association should be considered in each and every patient seen for symptoms of arterial insufficiency. A 77 year old white male was admitted to the hospital complaining of a severe burning intermittent claudication of the right leg of about 6 months' duration. A lumbar aortogram revealed a complete block at the bifurcation of the right common iliac artery. An endarterectomy was performed. Within 1 month following surgery, the patient complained of dysphagia. A diagnosis of carcinoma of the esophagus was confirmed. X-ray therapy was instituted, but the patient died of the latter disease 8 months after the vascular surgery.

During a recent visit to St. Bartholomew's Hospital in London, I was fortunate to make ward rounds with Sir James Paterson Ross and Dr. Fiorindo A. Simeone of Cleveland. At that time, this facet of peripheral vascular disease was discussed. Similar personal experiences were voiced at that time, representing three geographically widely separated areas. There is definite support, then, for a higher than generally suspected incidence of patients with signs and symptoms of arterial insufficiency who shortly manifest the clinical picture of a previously dormant but highly malignant carcinoma.

The sequence of events which leads to the possible association of these two disease processes is not well understood. Secondary enzymatic or protein changes in the blood in

cases of carcinoma may lead to an alteration in blood clotting as a possible causative mechanism. Carcinoma of the esophagus, stomach, and colon are known to be present in a silent manner for long periods, the patient finally presenting himself with severe anemia. It would seem highly probable that in the elderly patients with borderline lower extremity circulation, tissue ischemia, manifested as intermittent claudication, may be the first symptom or sign to become apparent in the progression of the carcinoma process. We must ever be on the alert for this contingency.

PERFORATION OF THE GALLBLADDER

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THE QUESTION of early versus delayed operation for acute cholecystitis would be a less controversial one if there were more general agreement concerning the frequency with which the acutely inflamed gallbladder perforates. Some surgeons believe that this is a common and serious complication. Others contend that it is a relative rarity, and that even when it does occur it is unlikely to prove dangerous because the inflammatory process usually in confined to the subhepatic space by adherent omentum, transverse colon, and other contiguous structures.

A recent review of an 18 year experience with acute cholecystitis at the Charity Hospital in New Orleans indicated that rupture of the gallbladder was found at operation or autopsy in 72 of the 1,060 patients. Of 679 patients operated upon, 9.3 per cent had a perforation of the gallbladder. This figure is a conservative one because it includes only those cases in which the operative note specifically described the presence of a gross defect in the gallbladder wall. Perforation into the free peritoneal cavity with generalized bile peritonitis was encountered in 21 (3 per cent) of the surgical cases, and one-third of these patients died. The perforation was localized to the pericholecystic area in 30 cases (4.4 per cent), and the mortality in this group was 16 per cent. Perforation into an adjacent viscus occurred 14 times (2.1 per cent), and was attended by a mortality of 21 per cent. Among the patients submitted to operation the mortality rate was 3 times as high in the group with perforation of the gallbladder as it was in the group in which the gallbladder wall appeared to be intact.

One can only speculate concerning the frequency with which rupture of the gallbladder occurred among the patients who were not operated upon. It is of interest that postmortem examination was performed in 14 of the 21 conservatively treated patients who died, and 6 of them were found to have free perforation of the gallbladder with generalized bile peritonitis.

There were 68 deaths among the 1,060 patients comprising this Charity Hospital series, and gross perforation of the gallbladder was demonstrated at operation or autopsy in one-third of these fatal cases.

It is suggested that, at least in this institution, perforation of the gallbladder is an important complication of acute cholecystitis.

THE SURGEON AT WORK

AN INCISION FOR THE REMOVAL OF STONES IMPACTED IN THE LOWER URETER

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THE HUMAN URETER, being 10 inches in length, requires an assortment of incisions for surgical exposure. To the surgeon, no portion is less accessible than that next the bladder. That some surgeons choose to approach this portion through a midline suprapubic incision while others, confronted with the same problem, prefer an oblique groin incision suggests that an ideal approach to the deep pelvic portion of the ureter has yet to be described. Our experiences with an alternative route are described in the present article.

In using the Cherney incision to perform various intrapelvic operations, it became apparent that a unilateral Cherney incision would afford excellent exposure of the lower ureter. Then, while employing the "half-Cherney" for this purpose, it became further apparent that fair exposure of the lower ureter could be obtained without dividing the insertion or any portion of the rectus muscle. Further slight refinements are responsible for the incision which is here described.

Operating experience has made manifest that this new incision has sharply restricted application. It is best chosen for the removal of impacted stones in the lower fifth (that is, the distal 2 inches) of the ureter. It may also be used preferentially for the division of the terminal ureter when the total operation planned is nephroureterectomy. This incision should *not* be used for: (1) any plastic procedure on the ureter, (2) vesical reimplantation of the ureter, or (3) removal of a ureteral remnant as a secondary operation. I have performed all of these procedures through this incision, and am convinced that wider exposure for such operations must be attained. Primarily then, and almost exclusively, this is an abdominal extraperitoneal incision for the removal of impacted stones from the lowermost ureter. However, since this is by far the commonest operation performed on the terminal ureter, it is believed that a technique which has been found narrowly useful may be of value to other surgeons.

FIG. 1. Roentgenogram of abdomen showing ureteral calculus in the ideal position for the incision described.

From the Urology Section, Surgical Service, Veterans Administration Hospital, New York.

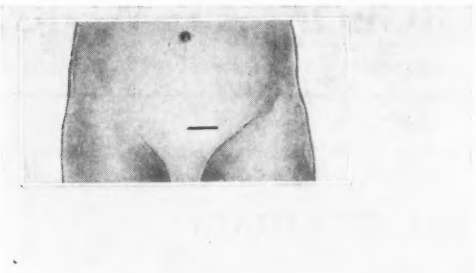


FIG. 2. Illustration showing the skin incision.

As a prelude to operation, the bladder is distended, via an inlying Foley balloon catheter, with 6 to 10 ounces of sterile water. After the bladder wall is visualized, the distending fluid is drained by an operating room assistant. Failure to empty the bladder at this stage of the procedure will greatly hamper deep visibility.

The skin incision (Fig. 2) is made horizontally 1 centimeter above the pubis, beginning just beyond the midline and extending laterally for from 7 to 8 centimeters. An incision in the same direction and of the same length is made through the anterior sheath of the rectus muscle and continued laterally to divide the contiguous portion of the aponeurosis of the external oblique muscle and the underlying parallel muscle fibers of the internal oblique and transversus abdominis, which, in this region of the abdomen, pass anteriorly to the rectus muscle (Fig. 3).

The transversalis fascia, adjacent to the lateral edge of the rectus muscle, is then punctured with the point of the dissecting scissors. The fascial rent is enlarged by lateral spreading, the limit of extension being the inferior epigastric vessels, which do not require division but which may be sacrificed without harm. With the rectus muscle retracted upward and medially, the fat which fills the space lateral to the bladder is easily parted from the external iliac vessels and the superior pubic ramus, thus exposing the lateral bladder wall (Fig. 4), and, in the depths, the periureteral fat. Any retractors placed laterally in the wound must be handled with care and gentleness, for the external iliac vessels will be compressed against the bony pelvis, and the risk of injury is ever-present.

If a stone is present in the ureter, the palpating finger-tip will handily find the ureter in the depths of the incision. When the ureter can be thus identified by touch, further dissection is neither beneficial nor needed. If the area of the impacted stone cannot be identified tactilely, delicate dissection of the fat surrounding the terminal ureter adjacent to the bladder will uncover the characteristic ureteral serosa, along which dissection may be continued to the site of the calculus.

The stone-containing ureteral segment (Fig. 5) is isolated between thumb and forefinger (or between forefinger and the bony pelvis). A longitudinal incision is made in the overlying ureteral

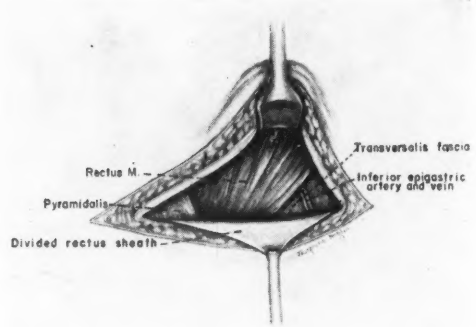


FIG. 3. Transverse incision in rectus sheath showing pyramidalis and rectus muscles, inferior epigastric vessels, and the transversalis fascia.

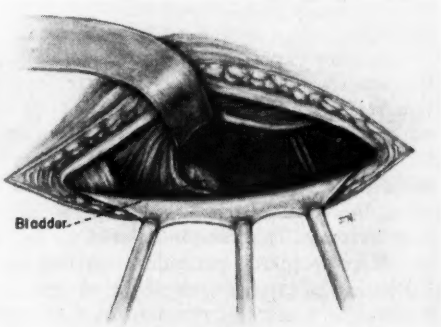


FIG. 4. The rectus muscle is retracted upward and medially to expose the bladder wall and fat overlying the ureter.

wall (insert, Fig. 5). The stone is delivered or extracted with gentle pressure and a suitable Randall forceps. All this is advisedly done without dissection of the ureteral circumference. Application of forceps of any kind to the ureter for fixation is unnecessary, and sometimes harmful.

Retractors are placed as needed; usually, a narrow Deaver is ideal for medial retraction of rectus muscle and bladder wall (Fig. 4). Richardson retractors of appropriate sizes are used superiorly and laterally as required. In every operation visual incision of the ureter has been achieved, and nothing less should satisfy the careful surgeon. At the site of an impacted stone the ureter tears easily and inadvertent disruption of ureteral continuity is not unknown.

The ureteral incision is not closed by suture. Good drainage of the impacted site is fostered by an open ureteral wound, which perhaps heals better and with less scar than when sutures are used. If there is troublesome postoperative urinary leakage from the wound (a complication which is not uncommon whenever ureteral stone is removed by open operation through any incision), an inlying ureteral catheter, No. 5 or 6 French caliber, inserted via the cystoscope, should afford immediate cessation.

After the stone is removed, a narrow Penrose drain is placed to the ureteral incision and brought out the lateral angle of the abdominal wound. The retractors are removed, permitting the bladder and the rectus muscle to fall back into anatomic relationship (Fig. 6). Interrupted sutures of No. 000 chromic catgut are taken to approximate the severed edges of the rectus sheath (Fig. 7). The skin incision is closed with interrupted Stewart sutures of No. 000 black silk. The drain is sutured with No. 000 silk to the skin edge, and a small safety pin is inserted in the external portion of the drain for the usual reasons. The skin sutures and the Penrose drain are removed on the seventh postoperative day. No attempt has been made to close the divided edges

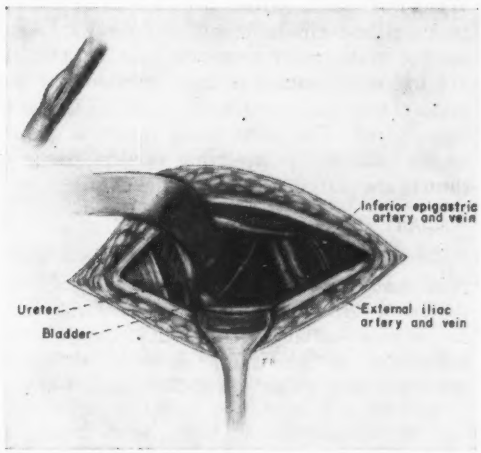


FIG. 5. The external iliac vessels are exposed by dissection of the overlying fat. Inset shows incision in ureteral wall.

of the transversalis fascia, for it has been thought that proper wound drainage required that this layer be left open. No instance of dehiscence or hernia has followed this technique.

When nephroureterectomy is planned, this incision may be used to approach the terminal ureter, either before or after the renal portion of the operation has been completed. It is my preference to divide the terminal ureter initially, since such staging better permits radical transperitoneal nephrectomy (removal of all perinephric fat, Gerota's capsule, and lymphatic tissue en bloc with the affected kidney). However, a lumbar approach may be combined with the described incision to accomplish a routine simple nephroureterectomy. When the latter combination is chosen, the lumbar incision and division of the renal vessels should ordinarily precede division of the terminal ureter.

Most genitourinary surgeons excise a portion of the trigone when ureterectomy is performed for transitional cell carcinoma of pelvis or ureter.

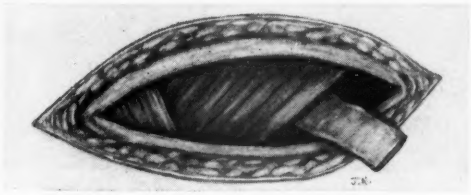


FIG. 6. Drain in position after removal of calculus. Note anatomic repositioning of the muscles.

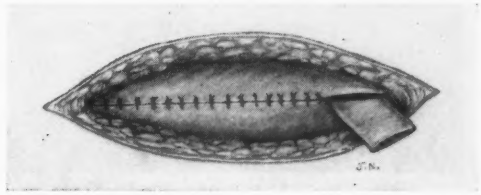


FIG. 7. Illustration showing the closure of the rectus sheath.

When this is intended the ureter should, of course, be mobilized circumferentially, traction being applied to the ureter to tent the bladder in which a purse-string suture is then inserted. As the ureteral traction is continued, a cuff of bladder is circumcised. The purse-string suture is drawn snugly, and a few inverting vertical mattress sutures are placed to reinforce the closure.

SUMMARY AND CONCLUSIONS

An incision is described for a single surgical procedure, namely, the removal of stones from the lower fifth of the ureter. The essential steps are: transverse lateral suprapubic incision, retraction of the rectus muscle medially, incision of the transversalis fascia, and localization of the ureter in the lateral paravesical space. This incision provides: simplicity of technique, avoidance of muscle and nerve transection, satisfactory exposure for a single surgical purpose, pathway for direct adequate drainage, and solid rapid wound healing with slight scarring.

Narrow indications are recommended, and the incision is not advised for more extensive procedures.

The incision has been used in 4 total nephroureterectomies, 6 ureterolithotomies, 1 excision of a ureteral remnant, and 1 reimplantation of a ureter damaged in hysterectomy.

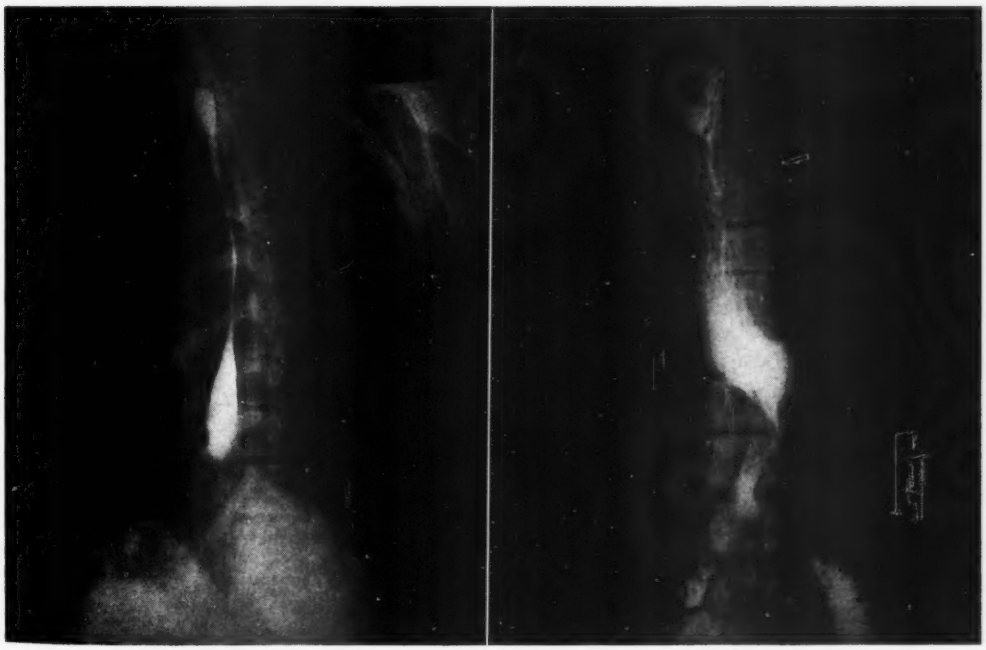
There have been no deaths, fistulas, nor hernias, and all wounds have healed promptly and securely.

RIGHT THORACOABDOMINAL APPROACH TO ESOPHAGEAL RESECTION

G. H. LAWRENCE, M.D., F.A.C.S., Seattle, Washington

THE ANATOMIC EASE with which the esophagus is approached through the right chest in lesions involving its middle third has provided a stimulus for varied combinations of thoracic and abdominal incisions, the latter being required to mobilize a portion of the gastrointestinal tract for esophageal replacement. Early reports favored staging the right sided approach, yet even as a one stage procedure, the disadvantage of time-consuming, separate abdominal and thoracic incisions detract from the desirability of a right sided thoracic approach. Unless the policy is adopted that all malignant esophageal lesions should be resected or by-passed, dilemma arises as to whether the chest or the abdomen should be explored first, as either may contain metastatic or nonresectable malignant lesions. Synchronous exploration by 2 surgical teams tends to decrease the operating time but is associated with a compromise of operating facility with crowding of personnel. The right thoracoabdominal approach obviates many of these disadvantages while providing an anatomically direct approach to the midesophagus. Mobilization of the aortic arch is unnecessary. Direct visualization of the bronchial and vascular components of the right hilus enables a safe dissection of the lesion from these structures, particularly the right inferior

From the Department of Surgery, The Mason Clinic, Seattle Washington.



a b

FIG. 1. a, Preoperative esophagram showing stricture of the esophagus caused by lye. b, Postoperative film showing stomach anastomosed to esophagus at level of first rib by use of a right thoracoabdominal approach.

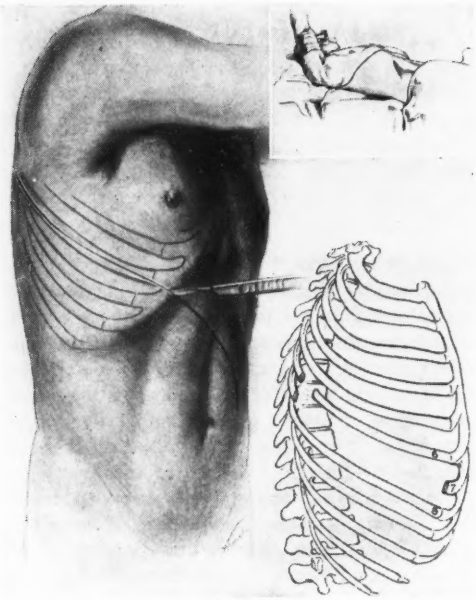


FIG. 2.

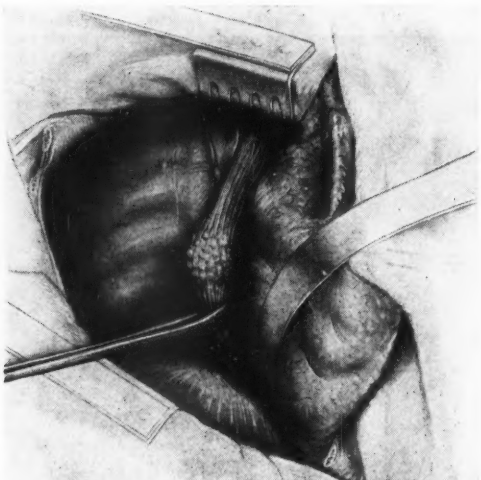


FIG. 3.

pulmonary vein. The level of esophageal transection is not compromised by the aortic arch, nor is its mobilization necessary.

As the stomach has usually been used to reestablish alimentary continuity, experience with this exposure has demonstrated the ease with

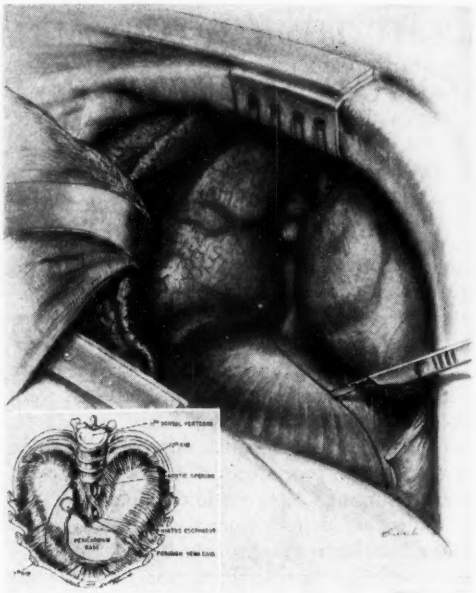


FIG. 4.

FIG. 2. A right sided anterolateral incision is carried from the posterior axillary line to the left paraumbilical area. The seventh rib is resected subperiosteally as are posterior portions of adjacent ribs when necessary. The costal margin is divided. The inset shows positioning of the patient upon the operating table.

FIG. 3. The esophagus is mobilized after division of the azygos vein.

FIG. 4. The diaphragmatic incision is placed lateral to the inferior vena cava as pictured more clearly in the inset. The inferior pulmonary vein is pictured semidiagrammatically to show its close relationship to the esophagus.

which this procedure is carried out. A more vertical extension of the abdominal component has permitted mobilization of the right colon for esophageal substitution in 1 case in our experience. Postoperative ileus following gastric mobilization is reduced as extensive handling and packing of the abdominal viscera are unnecessary. Redraping and repositioning of the patient are avoided with resultant saving of time in an otherwise lengthy procedure.

The right thoracoabdominal approach has been favored by several groups. The technical aspects of this approach to lesions of the middle and upper thirds of the esophagus, either benign or malignant, are discussed in this report. Two of the resections were performed for corrosive strictures of the esophagus (Fig. 1), the remainder for carcinoma.

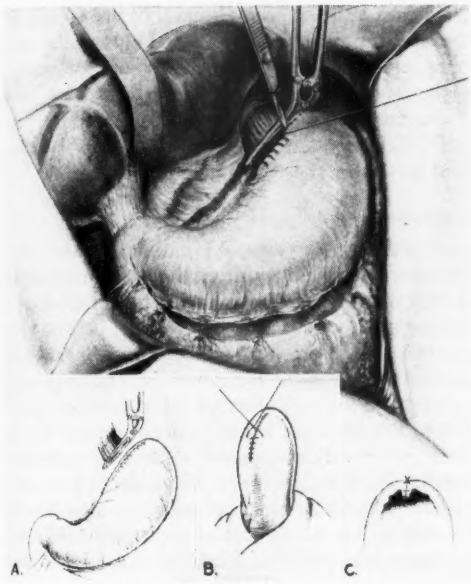


FIG. 5.

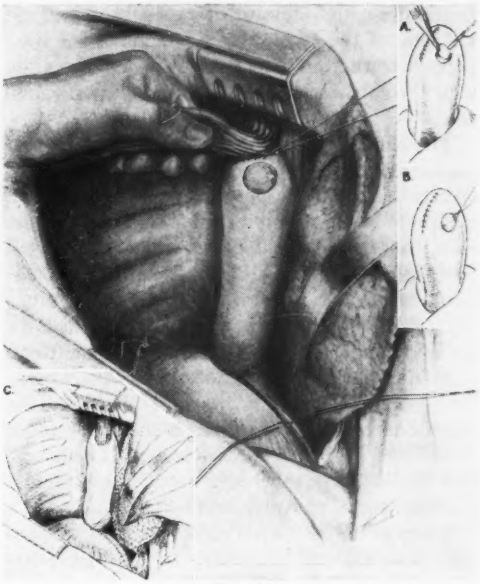


FIG. 6.

FIG. 5. The stomach is mobilized following resection of the triangular ligament of the liver which is then retracted toward the thorax through the diaphragmatic incision. The cardioesophageal junction is closed as depicted in the insets.

FIG. 6. The stomach is brought through the esophageal hiatus and a 3 layer esophagogastric anastomosis is performed on the anterior portion of the cardia. Insets A and B, Preparation of the stomach for esophagogastrostomy by removal of a serosal button. Inset C, Suture fixation of the stomach at the hiatus following closure of the diaphragm.

TECHNICAL CONSIDERATIONS

In preoperative evaluation, the local esophageal disease is visualized and biopsied endoscopically. Bronchoscopic evaluation of tracheal and bronchial involvement, as well as of vocal cord motion, should be obtained. Realizing that resection offers the best palliation in lesions of the thoracic portion of the esophagus, we have tended to explore even those lesions which give clinical evidence of local extension and in 1 instance have merely by-passed the local lesion.

The patient is positioned on the operating table at an angle of 30 degrees by placing sand bags beneath the shoulder and pelvic girdle. It is important to prepare the skin and to drape the patient so that the entire length of the thoracoabdominal incision will be available without further effort. An anterolateral thoracic incision is made over the seventh rib from the posterior axillary line to the costal margin (Fig. 2). Subperiosteal excision of the seventh rib provides excellent exposure for evaluation of the resectability of the esophageal lesion. Should it be technically helpful, resection of posterior segments of adjacent ribs will give added exposure, particularly for the performance of an anastomosis high on the esophagus (Fig. 2).

With the lung retracted anteriorly, the overlying azygos vein is divided and the esophagus mobilized with particular attention given to the contiguous right pulmonary vessels. This mobilization requires division of the inferior pulmonary ligament in order to obtain adequate exposure of the distal esophagus and esophageal hiatus.

Once the esophagus is mobilized (Fig. 3) and resectability determined, attention is then turned to mobilization of the stomach. An oblique epigastric incision in the abdominal wall permits excellent exposure for this purpose. The costal margin is divided in the line of incision which is then carried across both rectus abdominis muscles. In order to obtain better exposure in the area of the esophageal hiatus, it is necessary to divide the diaphragm at its anterior border in a line directed posteriorly and lateral to the inferior vena cava (Fig. 4). The length of this incision de-

pends upon the amount of exposure necessary. Division of the triangular ligament of the liver permits retraction of its left lobe when dissection near the cardioesophageal junction is performed (Fig. 5).

The stomach is mobilized in the conventional manner with preservation of the gastroepiploic vessels and the right gastric artery to insure an adequate blood supply to the stomach. Splenectomy has been avoided in upper esophageal lesions whenever possible and is usually technically unnecessary with the excellent exposure obtained. Pyloroplasty and pyloromyotomy have been reserved for those cases in which there seemed to be palpable evidence of obstruction in the pylorus. The esophagus is divided, and the distal end of the stomach is turned in by using No. 00 catgut sutures for the deeper 2 layers and No. 4-0 silk for the superficial layer (Fig. 5). While Hollingsworth cautions against the use of the esophageal hiatus for passage of the stomach into the chest, manual dilatation of the hiatus has proved a readily accessible and nonobstructing route for the stomach. With completion of the abdominal phase the rib spreader is reinserted more posteriorly, and an esophagogastric anastomosis is performed. Convinced of the safety of the 3 layer silk anastomosis as advocated by Sweet, I have been using this method exclusively. After preliminary fixation of the stomach in the chest with silk sutures, a round button of gastric serosa is removed from the area to be anastomosed. A posterior row of No. 4-0 silk is then placed at a distance of about 0.5 centimeter from this point (Fig. 6). The second layer incorporates only the muscularis of both organs. The third or mucosal layer approximates mucosa only with all the knots tied so that they lie within the anastomotic lumen. A previously inserted Levin tube is passed through the anastomosis prior to its completion for postoperative decompression.

With completion of the anastomosis, the diaphragm is closed in 2 layers with No. 00 silk, and the stomach is sutured to the diaphragm at the hiatus with serosal stitches of No. 000 silk. It is important to suture the severed costal margin with No. 26 gauge wire in order to avoid its subluxation as occurred in 1 case in which silk alone was used. This was of cosmetic significance only. The chest and abdominal incisions are closed in the usual manner after a lateral chest tube has been placed in the ninth interspace for water sealed drainage. The entire procedure has averaged 3½ hours in the usual case, and the patient has adequate intestinal function to start oral intake by the third or fourth day.

RESULTS

In the past 4 years, 13 patients have been operated on by using this method with technical satisfaction. There have been 2 postoperative deaths from coronary occlusion proved at autopsy. There were no anastomotic leaks. One patient suffered a transient brachial plexus palsy from hyperabduction of the right arm. There has been no wound infection, but 1 patient, previously mentioned, suffered a subluxation of the costal margin. No patients have required secondary pyloric drainage despite its infrequent use at the initial procedure. Watson and associates report a mortality rate of 24.4 per cent using the right sided thoracoabdominal approach for performing esophageal resection in 45 cases.

CONCLUSION

The right sided thoracoabdominal approach to resection of the middle and upper thirds of the esophagus provides an expeditious, technically practical technique. Time is saved because repositioning and redraping of the patient are unnecessary. Thoracoabdominal exposure avoids excessive manipulation of the abdominal contents. The right sided approach readily exposes the esophagus and its relationships. Anatomic limitations imposed by the relationship of the liver and inferior vena cava to the right diaphragm are not actually significant, for this approach is not selected for lesions located near the cardioesophageal junction.

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A NEW TECHNIQUE FOR BLADDER RECONSTRUCTION

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ROBERT BOWER, M.D., and DAVID M. LONG, JR., M.D., Philadelphia, Pennsylvania

THE NEED FOR A URINARY BLADDER SUBSTITUTE which satisfies the rigid criteria for satisfactory physiologic performance is self evident. Efforts in the past have been directed toward methods of diverting the urine to the exterior by by-passing the bladder. More recently, interest has centered around methods of developing bladder substitutes.

The earliest recorded instances of urinary diversion date from the writings of Hippocrates who noted the accidental occurrence of urinary fistulas after nephrolithotomy. John Simon made the first deliberate attempt to divert the urinary stream over a hundred years ago. In a patient with exstrophy of the bladder he transplanted the ureters into the rectum with temporary success. The succession of efforts to achieve safe and effective urinary diversion in the past century have included the following procedures: nephrostomy, pyelostomy, ureterocutaneous transplantation, ureterocolpostomy, ureteroureterostomy, ureterotransverse-colostomy, ureterosigmoidostomy and ureteroproctostomy. Many of these methods still have their advocates today.

A second phase in the history of ablative surgery of the bladder has been the development of techniques for bladder substitutes. The numerous types of proposed artificial bladders have resulted from combinations of the following factors: The ureters have been transplanted into isolated segments of intestine, including the ileum, ileocecum, cecum, sigmoid, and rectum. These intestinal loops have then been anastomosed to the bladder neck, brought out through the abdominal wall or the anal sphincter, with or without subsequent colostomy to divert the gastrointestinal tract.

In general, bladder substitutes may be classified as follows: (1) intestinal segments which act primarily as conduits with no attempt to provide reservoir function; (2) intestinal loops which are primarily concerned with providing a reservoir for the urine but require intermittent catheterization; (3) procedures which use the anus and rectal ampulla, or a transposed segment of intestine brought through the anal sphincter in an effort to provide urinary continence; (4) techniques using intestinal loops anastomosed to the urethra or bladder neck.

The difficulties and complications which have followed ureteral transplantation or the formation of artificial bladders include: wearing of collection bags; infection with ascending pyelonephritis; stricture formation; absorption of electrolytes, urea, and nitrogenous wastes, producing hyperchloremic acidosis and uremia; and secretion of mucus and other irritating substances or enzymes by the bladder substitute which may prevent permanent bacterial sterilization. In some instances fewer long term survivals have been observed after radical surgery for bladder carcinoma than after the more conservative measures. We believe that although intestinal segments may have many salutary advantages in bladder substitution, the inherent functions of the intestinal mucous membrane preclude ideal clinical results.

Our approach has been an attempt to reconstruct the bladder in a manner which would simulate, as closely as possible, the normal anatomy and physiology. To this end we have reconstructed the subtotally and totally resected bladder in the experimental animal (2, 4). Of the 5 types of intestinal grafts studied, the reversed seromuscular ileal graft gave the best results under experimental conditions. Within 2 or 3 weeks the latter graft became lined with stratified transitional cell epithelium; the two-layered muscular architecture of the intestine broke up into smaller muscular bundles which gradually became interlaced in a plexiform network morphologically indistinguishable from the normal detrusor muscle (4). Normal function of the bladder reconstructed with this graft was demonstrated by the observed micturition patterns, satisfactory capacity, absence of residual urine, cystograms, intravenous pyelograms, retrograde

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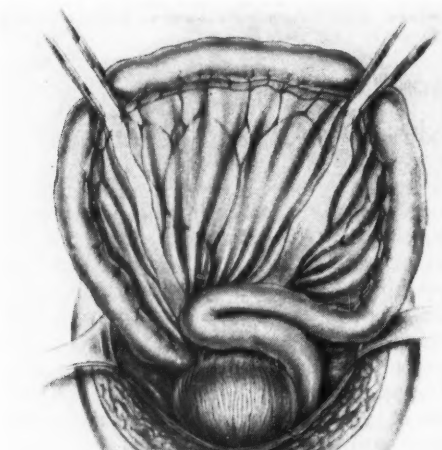

FIG. 1.

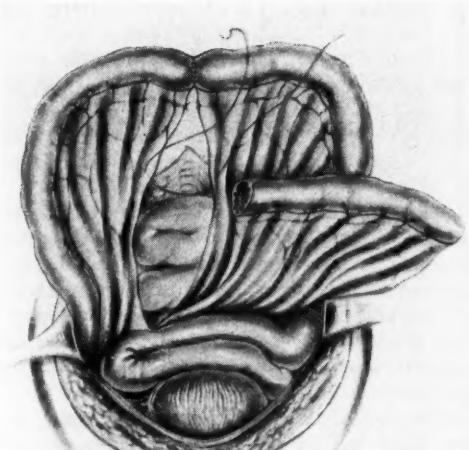

FIG. 2.

FIG. 1. The abdomen is opened, the bladder exposed, and a segment of ileum with its intact mesentery is isolated.

FIG. 2. The intestinal tract is anastomosed and the mesenteric defect closed.

urograms, and cystometrograms. Instillation of radioactive isotopic ions (Na, I, and PO_4) into into this type of reconstructed bladder demonstrated ion transport patterns comparable to the normal, whereas in bladders reconstructed with the classically described mucous membrane-lined ileal grafts significant absorption occurred (2). The innervation of this type of reconstructed bladder has been studied and its application to the treatment of the neurogenic or denervated bladder has been investigated in the experimental animal (1, 3).

TECHNIQUE

The approach is through a conventional midline or paramedian incision made from a point approximately 4 or 5 centimeters above the umbilicus to the symphysis. The peritoneum is opened, the retropubic space and bladder are exposed, and the terminal ileum is brought up into the mouth of the wound. A 35 centimeter ileal segment whose mesentery is pendulous and situated nearest the pelvic organs is selected. Preferably, the mesentery should contain a sizable branch or branches of the ileal or ileocolic vessels. Both sides of the intestinal segment are doubly clamped with intestinal instruments and divided (Fig. 1). The mesentery opposite each bowel transection is divided posteriorly down to its attachment so that the isolated segment now hangs freely on a mesenteric pedicle. Care is taken to preserve the integrity of the vascular and neural connections coursing through the pedicle. The continuity of the intestinal tract is re-established by means of an end-to-end or side-to-side anastomosis and the defect in the mesentery is closed with interrupted sutures (Fig. 2).

From this isolated pedicled intestinal segment a reversed seromuscular graft is made by first incising the anterior wall of the intestine about 1 centimeter from the mesentery (Fig. 3a), and then opening it out into a sheet (Fig. 3b). The mesenteric attachment lies close to one edge. Bleeding points may be controlled with ligatures of No. 000 plain catgut and warm moist packs.

The mucous membrane can be elevated by careful dissection between the layers of the intestinal wall; a cleavage plane is found either between the mucosa and submucosa or between the submucosa and the muscularis. When only the mucosa is removed, (the raw submucosa remaining to face the exterior of the newly reconstructed organ), meticulous care must be taken to evert the edges of the graft when suturing it to the

bladder remnant. If a small tuft of the raw submucosa is inverted along with the anastomotic border, deeply situated ileal mucosal epithelium will overgrow the graft, outstripping the slower growing urothelium. Similarly, care must be taken to use only a seromuscular stitch on the graft, instead of a full thickness stitch, as ileal mucosal cells may be drawn through on the needle and implanted along the suture line. These problems are obviated if the submucosa, as well as the mucosa, is removed. Removing all the mucosa theoretically may be sufficient, but we have found experimentally that the ileal epithelium is difficult, if not impossible, to remove completely without also taking the submucosa layer. Despite all mechanical efforts to irradicate them, some mucosal cells persist especially over Peyer's patches where lymphoid infiltration of both layers make separation difficult. Therefore, we have found that removing both mucosa and submucosa eliminates this hazard altogether. The graft is rather thin and somewhat friable since strength and substance lie in the tough submucosal layer. Initially, we were reticent to use such a flimsy graft, but biopsy specimens taken a few months postoperatively demonstrated no discernible difference between the two types of grafts.

After the mucosa and submucosa are removed leaving only the seromuscular coat and its attached mesentery (Fig. 3c), the graft is then reversed or turned upon itself so that the smooth sterile serosa is then facing uppermost (Fig. 3d).

The long narrow graft is fashioned into a hollow spherical viscus by the following series of steps: One end of the graft is folded transversely onto itself in such a manner that the serosal surfaces face each other (Fig. 4a). These surfaces are united with a continuous No. 00 chromic catgut suture along a line approximately 1 centimeter from the mesenteric border. This union forms a trough or "hod" shaped structure at one end of the graft (Fig. 4a). A similar serosa-lined hod is fashioned at the opposite end of the graft (Fig. 4b). Thus the mesentery, which is attached to one edge of the graft, is excluded. Sutures are taken parallel to the blood vessels (i.e., transverse to the long axis of the bowel) to preserve the maximal vascularity.

Attention is now turned to the bladder and a total or subtotal cystectomy is performed according to the operative indication (Fig. 4c). This

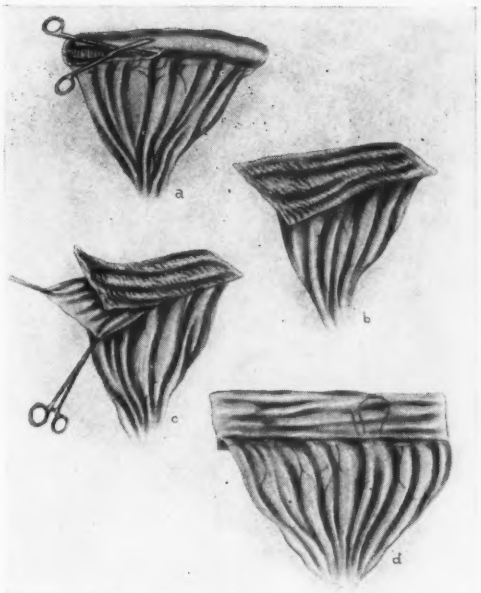

FIG. 3. Preparation of the graft. a, The anterior wall of the ileal segment is cut along the mesentery (viewed from above). b, The ileal segment is opened out into a sheet (viewed from above). c, The mucous membrane and submucosa are elevated and removed (viewed from above). d, The graft is reversed or turned up so that the serosal surface faces the operator (viewed from below). The suture is started at one side of the graft.

step may be done by a second surgical team at the same time that the graft is prepared in order to minimize operative time. If a cystectomy is required, the graft is sutured to the urethra or bladder neck and the ureters transplanted into the graft (cf. ref. 2, pp. 471–472 and Fig. 15). If the operator chooses to leave the trigone, as depicted in these illustrations, the graft may be readily united to it without transplantation of the ureters. The graft is brought down into the pelvis, and the center of the graft is united to the posterior margin of the bladder remnant by means of a continuous suture of No. 00 or No. 000 chromic catgut (Fig. 5a). The serosal surface now faces inward toward the lumen of the reconstructed organ, and the excluded mesentery remains attached to one edge of the graft. One of the hods is attached to each side of the bladder remnant by means of a continuous suture (Fig. 5b and c). Because of its greater length the border of the graft is gathered up or reefed as it is sutured to the bladder trigone.

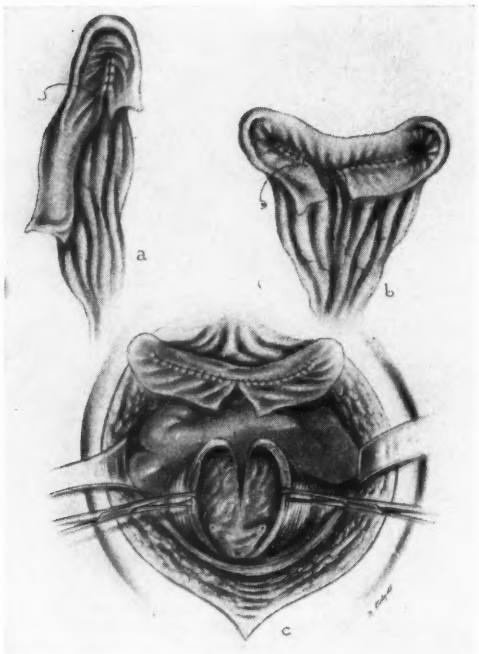

FIG. 4.

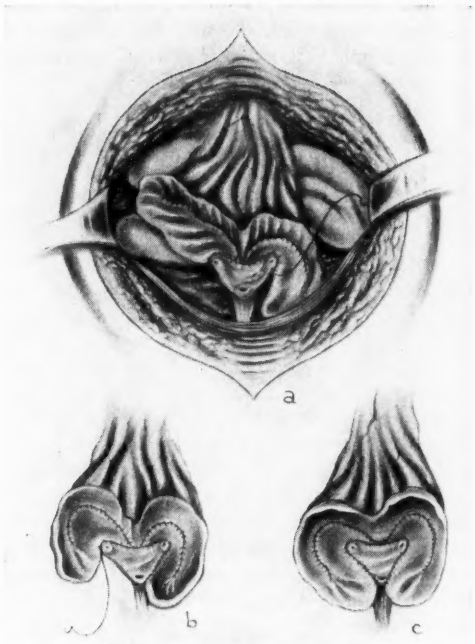

FIG. 5.

FIG. 4. a, The graft is folded transversely and the suture continued adjacent to the mesentery (but excluding the mesentery) in order to form a hod-shaped structure at one end. b, A trough or hod is similiarly fashioned at the opposite end. c, The bladder is opened and the completed graft brought down into the pelvis.

FIG. 5. a, The center of the graft is sutured to the posterior portion of the bladder remnant. b and c, Each side of the graft is sutured to the bladder neck or trigone.

The pliability and elasticity of the intestinal tissue allow the two hods or trough-shaped corners to assume the shape of hemispheres, which are then united in the midline inferiorly (Fig. 6a). The same suture is continued around anteriorly (Fig. 6b). A Foley catheter is introduced through the urethra. The suture then completes the union of the two sides of the graft anteriorly (Fig. 6c). After final inspection of the operative area, the Foley bag is inflated, a large Penrose drain is placed in the retropubic space, and the wound is closed in layers with interrupted sutures.

DISCUSSION

The reversed seromuscular graft, a viable pedicled segment of intestinal tissue, has been found to provide a convenient and feasible tool for bladder reconstruction. The graft material is readily available and easily mobilized; its elasticity and pliability allow it to be shaped into the general configuration of the bladder; the graft contains a functioning smooth muscle layer; it has intact neural and vascular connections; the graft allows overgrowth of transitional cell epithelium, which prevents resorption of electrolytes and nitrogenous materials; the graft does not secrete mucus or irritating substances.

Reconstruction of the bladder with reversed seromuscular grafts was accomplished in 4 clinical cases. As yet there has been no mortality:

The first operation was performed upon a 59 year old white male with carcinoma of the bladder over 3 years ago. This patient developed the only major complication of the series, a suprapubic fistula with antibiotic resistant organism, which persisted for several months but gradually subsided. The patient is now continent, has a normal micturition reflex, a capacity of about

6½ ounces, and absence of significant residual urine.

The second patient was a 63 year old negro female who was completely incontinent of urine for 22 years and suffered from recurrent bilateral nephrolithiasis during the past 5 or 6 years. The bladder capacity was 1 ounce. In this instance the bladder was not resected but, in an effort to increase the capacity, the graft was anastomosed to a small incision in the superior aspect of the bladder dome. The effort was unrewarding. In retrospect, 2 mistakes were made: the nonfunctioning or paralyzed detrusor muscle should have been removed; the opposing sides of the graft must be kept separated (as by a Foley catheter) until they become lined with urothelium, since peritoneal surfaces irritated and inflamed by urine may become adherent and sealed off. We have never seen this result either in animal or patient when the bladder was resected down to the trigone and the graft applied to a relatively wide base.

The third patient, a 9½ year old white female, had a congenital spina bifida with myelodysplasia, urinary and fecal incontinence from birth, and marked paresis of the muscles of the lower extremities. An attempt to repair the myelodysplasia was made at the age of 3 weeks. She had had attacks of acute pyelonephritis every few months during the past 3 or 4 years. When seen at this hospital she was noted to have a constant dribbling of urine and was obliged to wear diapers. After manual pressure over the suprapubic area she would remain dry for about an hour. The capacity of the bladder was 1 ounce; a cystometrogram showed a small contracted bladder with no sensation of fullness, pain, nor desire to void on forcible overdistention. Subtotal resection of the bladder and reconstruction were carried out. Shortly after recovery from anesthesia sensation was noted on gentle irrigation of the bladder catheter. It was described as a gas pain and was localized below the umbilicus and slightly to the right of the midline. The bladder was kept decompressed with catheter drainage for 3 weeks, following which, tidal drainage was used for 4 weeks to allow the patient to get used to the sensation of fullness and to gain some measure of control. The apparatus was set to empty at low pressures (6 cm.) and gradually raised as the newly reconstructed bladder developed increasing capacity. During this time the patient developed an acute episode of pyelonephritis which responded to antibiotics and temporary discontinuance of the tidal drainage. Following discharge from the hospital she slowly gained voluntary control of the micturition over a period of several months. As would be anticipated in a child who has never had any degree of continence, the learning of bladder control was not only slow, but also marked by periods of temporary remission. She now remains dry for periods up to 4½ or 5 hours during the day and has a capacity of approximately 4½ ounces.

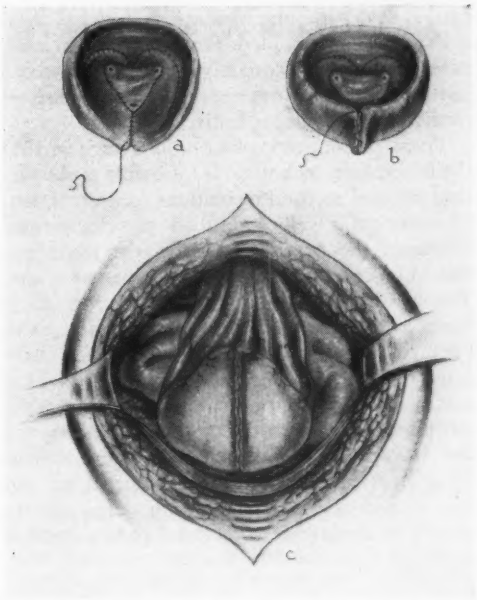

FIG. 6. a, The suture is continued so as to unite the hods of the graft in the midline posteriorly. b, This suture is continued anteriorly. c, The reconstruction is completed.

The last patient was an asthenic 25 year old white female who had had chronic interstitial cystitis for 10 years, as well as repeated episodes of acute pyelonephritis. A bilateral pelvic neurectomy was performed elsewhere after repeated conservative measures failed to give relief. Postoperatively she noted cessation of pain and other symptoms, but she was completely incontinent. Recurrent episodes of pyelonephritis (proteus) complicated matters. We were asked to see the patient at this time because of the troublesome incontinence. A resection of the denervated bladder and reconstruction were

carried out. Although insufficient time has elapsed for satisfactory bladder capacity or to evaluate the result adequately, she has had some control of micturition, except during periods of recurrence of pyelonephritis.

These preliminary observations suggest that the introduced technique is a feasible and practical clinical method of bladder reconstruction. The concept is well established on experimental evidence; the precise details of the technique should be considered in a developmental phase. The results, thus far, are encouraging. It is believed that the procedure may find a place in the management of vesical carcinoma, neurogenic bladder, the small contracted bladder resulting from healed tuberculosis or other specific infections, and interstitial cystitis. Of interest are the physiologic or neurophysiologic implications involved in substituting intestinal smooth muscle innervated by the vagus for vesical smooth muscle innervated by the sacral parasympathic nerves.

SUMMARY

1. The peculiar qualities of the reversed seromuscular intestinal graft make it an ideal source material for intraperitoneal reconstructive procedures.

2. A technique for functional, as well as anatomic, reconstruction of the urinary bladder using this graft is described with preliminary results and observations on 4 clinical cases.

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THE SURGEON'S LIBRARY

Reviews of New Books

No one who notes the names of the editors of *Surgery: Principles and Practice*[1]—J. Garrott Allen, Henry N. Harkins, Carl A. Moyer, and Jonathan E. Rhoads, and of their distinguished collaborators in special fields—would doubt that their combined efforts would result in a noteworthy textbook. When, furthermore, he catches a glimpse from the preface of the arduous time and effort the editors, who have themselves contributed one-half of the volume, put forth to achieve their aim he cannot help but realize that they put their hearts and souls into the task. The result fully justifies their efforts.

This new textbook is painstakingly and soundly documented on the surgical experience and investigations not only of the editors and of the contributing editors but also upon those of the many workers in every field of surgery to whom credit is given in the extensive bibliography that follows each chapter. The current views regarding surgical diagnosis and treatment are set forth in a 1,495 page volume which is exceedingly well organized and beautifully printed to permit ease in reading.

Throughout the first 307 pages the authors have most interestingly summarized the basic sciences as they apply to the field of surgery. The recent advances in medicine and surgery that have resulted from the development of the sciences of bacteriology, chemistry, and physics cannot be challenged, as one must realize as he reads the chapters pertaining to surgical bacteriology, fluid and electrolyte balance, nutrition, shock, and isotope techniques. The subject of anesthesia is carefully considered and discussed without comments upon the technical aspects of this field.

In the following 135 pages fractures and dislocations are discussed in an unusually appealing manner. This section includes a short chapter on surgery of the hand, which one could wish, in view of the importance of the subject, were more comprehensive.

The framework of this book lies in the 677 pages which are preceded by a chapter on military surgery. It presents an immense amount of material in a consideration of the specific regions of the body. Logically, the skin and subcutaneous tissue are discussed first and this section ends with a chapter on carcinoma of the lung and tumors of the thorax. Within the confines of these pages both student and experienced surgeon can enrich his knowledge since compactness and completeness have keenly sharpened the authors' pens.

The section on surgery of the thyroid, thymus, and parathyroids is extremely well written and represents an excellent summary of current information in this field. In general, the endocrine system is well reviewed and accepted principles are detailed. Including a 30 page chapter on the spleen, 376 pages are utilized to emphasize the surgical principles applicable to the gastrointestinal tract and accessory organs. The authors have used both line drawings and diagrams to simplify and reiterate many basic principles now accepted by the surgical profession. The section on anorectal lesions is very well done and the excellent diagrammatic drawings will help every student to understand better an area about which he is often confused. Hernia forms a postscript to the section mentioned. This important subject is discussed in masterly style and illustrated with excellent line and halftone drawings which emphasize the principles of repair of inguinal and diaphragmatic hernias. The less common hernias are also considered.

Approximately 48 pages are devoted to peripheral vascular surgery. The authors have covered this field in a simple but comprehensive manner.

With a similar method in both style and space cardiac surgery is presented. The author has carefully described lesions of the heart and great vessels and has used extreme open-mindedness in discussing the surgical correction of the various lesions considered.

A section of 64 pages covers the field of thoracic surgery, including the lung and thoracic cage. Pulmonary tuberculosis is given special attention, and, finally and properly, carcinoma of the lung and tumors of the thorax are presented in a concise but informative manner.

In 46 pages the principles of general plastic surgery are described and the authors have combined both photographs and line drawings to demonstrate, reiterate, and emphasize the fundamental surgical avenues to obtain desired reconstructive results. The general field is excellently described and specific details are simplified. Repair of a cleft lip is a good example.

[1]Surgery: Principles and Practice. Edited by J. Garrott Allen, M.D., Henry N. Harkins, M.D., Ph.D., Carl A. Moyer, M.D., and Jonathan E. Rhoads, M.D., D.Sc.(Med.). 1495 pages, 623 illustrations. $16.00. Philadelphia and Montreal: J. B. Lippincott Co., 1957.

A special section on pediatric surgery is included. Within these 37 pages the author describes the common lesions of the head and neck, the thorax, and the gastrointestinal tract to which infants and children are prone.

To make this new surgical volume complete the final sections of the textbook are devoted to the surgical specialties, namely, gynecology, urology, orthopedics, and neurosurgery. In these last 195 pages basic informative and modern ideas are presented. The authors have been conscious of their responsibility and have summarized their respective regions in an outstanding manner. No student or physician could possibly read these sections without being impressed by the simplicity of presentation and the basic philosophy contained therein.

This new surgical textbook is sound and embraces most of the surgical sphere as it is now conceived. In this reader's mind the editors have accomplished the important task which they proposed in their objectives. Unquestionably this treatise represents a task well done. It is highly recommended to every student and physician working in the field of surgery.

—Vinton E. Siler.

NIEBURGS' BOOK entitled *Cytologic Technics for Office and Clinic*[2] is designed to cover all the cytologic techniques applied in the diagnosis of malignancies, as well as hormonal activity, by a study of vaginal exfoliative cytology. The book is a product of laboratory experience and an extensive survey of the literature, and is closely tied to the needs of pathologists, cytologists, gynecologists, and general practitioners.

There are 26 chapters with good illustrations, the best being those dealing with the diagnosis of carcinoma of the cervix, in which the author points out modern concepts concerning the importance of the morphology of the malignant cells in relation to the prognosis before and after radiation therapy. All the statements are based on personal experience and supported by recent publications. Of particular interest is the evaluation of methods for obtaining cells from the cervix in correlation with the degree of accuracy in diagnosis. The chapter devoted to the procedures for estimation of hormonal activity has detailed illustrations and explanations. The mucus arborization test (Fern test) is briefly discussed.

An exaggerated estimate of accuracy is given to the cytologic method in the diagnosis of primary tumors by the examination of cells obtained from serous effusions and secretions. Such accuracy is probably achieved by extremely experienced cytopathologists but is beyond the limitations of the average pathologist. Some other techniques, such as those of surface abrasion methods in tumors of the colon and stomach are evaluated, but on the basis of a limited experience and few references.

The final chapters give important suggestions about mailing slides, training of personnel, and laboratory procedures. A complete bibliography is appended.

This book should serve as a useful reference volume upon this subject. *—Hector Marquez.*

[2]CYTOLOGIC TECHNICS FOR OFFICE AND CLINIC. By H. E. Nieburgs, M.D. 233 pages, 171 illustrations. $7.75. New York, London: Grune & Stratton, 1956.

CONGENITAL ANOMALIES of the viscera are common. They may present a clinical picture at birth or during the first few days of life which demands immediate surgical intervention; they may exist throughout a person's life and in no way impair his health; they may, in exceptional cases, cause trouble only in old age. They are, therefore, the concern of the obstetrician, the specialist in pediatrics, the family doctor, and very often the surgeon.

The clinical problem to which they give rise may be a very typical one, easily recognized, well understood, and easy of correction; it may be very obscure and may tax to the utmost the ingenuity and resourcefulness of the doctor in his effort to figure out a basic explanation; it may necessitate an extremely complicated and often a very hazardous surgical operation.

It is no wonder, therefore, that a new book of the caliber of *Congenital Anomalies of the Viscera*[3] will be received with enthusiasm by the medical profession. Its author, J. L. Bremer, Professor Emeritus of Anatomy at Harvard University, is an authority in the field of embryology, and, being closely associated with the work at the Children's Hospital in Boston, he has become familiar with clinical problems, many of which have their origin in some developmental defect. In his own words he has attempted in this book to "gratify a need of further knowledge of the later fetal or prenatal or even post-natal growths and abnormal possibilities as well as the normal sequences of developmental processes."

This little volume is clearly and simply written, but, as I have personally found out, it cannot be read in an evening like a dime novel. It requires many hours of careful study of the text and very close scrutiny of the many intricate diagrams and drawings, many of which have been used before in the author's previous publications on embryology, some of which have been taken from Dr. Gross' text on *The Surgery of Infancy and Childhood.*

In any event, the effort put forth in the study of this book will be very rewarding. *—Edwin M. Miller.*

DURING THE LAST FEW DECADES neurosurgery has progressed from the removal of tumors to the treatment or correction of functional troubles. In the book, *Neurochirurgie fonctionnelle*,[4] Pierre Wertheimer discusses the possibilities of surgical treatment of motor disturbances, pain, mental diseases, cerebral vascular changes, and of disturbances of the circulation of the cerebrospinal fluid. Most of the conditions the author discusses were not considered amenable to surgical treatment 30 years ago. Such treatment involves trials to correct functional troubles without treating their cause.

The first part deals with motor disturbances of the voluntary and involuntary nervous system, and includes tremor, dyskinesia, athetosis, and spastic paralysis of childhood. The anatomy, physiopathology, and surgical techniques are briefly discussed, and the

[3]CONGENITAL ANOMALIES OF THE VISCERA; THEIR EMBRYOLOGICAL BASIS. By J. Lewis Bremer, M.D. 202 pages, 89 illustrations. $5.00. Cambridge: Harvard University Press, 1957.

[4]NEUROCHIRURGIE FONCTIONNELLE. By Pierre Wertheimer Preface by Professor René Leriche. 186 pages, 46 illustrations. 1.500 fr. Paris: Masson et Cie, 1956.

author concludes his chapter by stating that definite conclusions have not yet been reached in this field. In the second part, the author reviews the techniques, the indications, and the results of the surgical treatment of epilepsy. The best chapter in the book concerns the surgical treatment of pain because of the particular knowledge the author has acquired in this field. He discusses its physiopathology, gives the principles of surgical treatment, and describes its multiple techniques. The last part of the volume describes the possibilities of surgical treatment of mental diseases, of cerebral vascular changes, and of disturbances of the circulation of the cerebrospinal fluid.

The book is a valuable analysis of the progress made during recent years in the solution of these problems. It contains an up-to-date bibliography and good schematic drawings. The surgical techniques, unfortunately, are poorly illustrated. The preface is by René Leriche. —*Robert Cote.*

THE MONOGRAPH entitled *Bladder Tumors*[5] is a reprint of a symposium which appeared in the June 1956, issue of *Cancer*. It presents an analysis of the combined experience of the New York and Memorial Hospitals with 1,065 cases of carcinoma of the bladder. Included in the studies presented are evaluations of the efficacy of treatment afforded by local excision and fulguration, segmental resection, simple cystectomy, and radical cystectomy or pelvic exeneration. The technique of radical total cystectomy as employed by the authors is presented in detail.

Throughout this series of papers, the tumors discussed are classified with regard to both stage and grade. Survival rates are presented with regard to the depth of infiltration and histologic appearance of the lesion. As a result of these studies, the authors point out that the grade and stage of a bladder tumor seems to influence the survival more than the type of surgical treatment. They conclude that pelvic exeneration has no place in the treatment of bladder tumors. The presence of more than one or two positive nodes is said to contraindicate radical surgery.

The authors favor radical cystectomy or radical segmental resection for tumors which have just invaded the perivesical space. They are inclined toward a vigorous surgical approach to the more deeply infiltrating high grade tumors confined to the bladder. The more conservative forms of therapy are recommended for the superficial tumors of the bladder. Despite this group of recommendations, there seems to be little positive evidence in this series of observations to engender enthusiasm for a radical surgical approach to carcinoma of the bladder.

This is a carefully documented monograph which presents concisely and clearly the results of a broad experience with bladder tumors. Although the authors have presented opinion as well as factual evidence in these papers, they have constantly distinguished the two. This publication is highly recommended for all who must advise and treat patients with tumors of the urinary bladder.

—*John T. Grayhack.*

[5]BLADDER TUMORS; A SYMPOSIUM. By Mitchell Brice, II, M.D., James L. Green, M.D., John J. Harris, Ph.D., Jack Holden, M.D., Gustavus A. Humphreys, M.D., K. T. Ma, M.D., Victor F. Marshall, M.D., J. Alan Nichols, M.D., Albert J. Paquin, M.D., George R. Prout, M.D., Samuel I. Roland, M.D., and Willet F. Whitmore, Jr., M.D. Philadelphia: J.B. Lippincott Co., 1957.

THE TEXTBOOK entitled *Operative Surgery*[6] consisting of 853 pages is divided into 28 chapters and encompasses the entire field of surgery. The method of presentation of the material includes a brief review of the surgical anatomy involved, the indications for surgery, the choice of procedure, and, in some instances, preoperative and postoperative treatment is discussed. There are ample and excellent illustrations of the surgical procedures described, and a total of 623 figures augment the text. The purpose of the book, as stated by the author, is to present, from the viewpoint of the general surgeon, all the operations that the junior in general surgery is likely to undertake, or in which he may have to assist. In addition, such specialized procedures as he may be required to do, when more expert help is not available, are included. Thus, the material includes general abdominal surgery, neurosurgery, orthopedic surgery, and genitourinary surgery.

In general, all standard surgical procedures are clearly presented in conformity with the most recent knowledge on the subject. Some recommendations may be controversial, but, in most instances, the fact that there is controversy is made apparent. Some of these recommendations follow:

1. The use of sulfonamide and penicillin dusting powder is suggested in a traumatic skin flap before it is sutured in place (page 186).

2. Simple mastectomy combined with radiotherapy is advised in the treatment of carcinoma of the breast (page 366). Statistics from the Royal Infirmary of Edinburgh are presented to indicate that the 5 year survival rate is better in patients treated by this method, than by the method of radical mastectomy, either with or without radiotherapy.

3. Carcinoma of the esophagus (page 399) is stated to be "one of the less aggressive malignant tumors, and for a long time it is no more than locally invasive." The wide unsuspected submucosal spread these tumors often exhibit, when the surgical specimen is examined, does not seem to warrant this opinion.

4. The use of gastrojejunostomy alone (page 457) is advised for: "a, patients between 35 and 55 with pyloric stenosis associated with low acid values in the gastric juice; b, patients over 55, with or without stenosis, but again with low acid values."

There may be considerable doubt in the minds of some, as to whether these are wise recommendations, considering the known incidence of marginal ulcer after gastrojejunostomy alone, in spite of apparent acid values.

This book seems to fulfill the purpose for which it was written, and would supply a useful reference for the surgical resident in training.—*Lawrence Chaffin.*

MORPHOLOGY has long been the cornerstone of hematology, and in the 629 pages of the quite remarkable

[6]TEXTBOOK OF OPERATIVE SURGERY. By Eric L. Farquharson, M.D., F.R.C.S. (Ed.), F.R.C.S. (Eng.). 853 pages, 623 illustrations. $15.00. Edinburgh and London: E. & S. Livingstone Ltd.; Baltimore: The Williams & Wilkins Co., 1954.

book, *Cytology of the Blood and Blood-Forming Organs*,[7] Dr. Bessis has brought morphologic hematology forward in giant steps. Though he has retained some of the descriptions familiar to classical hematology, he has largely confined himself to a presentation of the living blood cells and their ultra structure as defined by the advanced methods of electron and phase microscopy. Much of the work presented is the author's own, and it serves as an insight into the skill of this investigator.

Part 1 of the book (5 chapters) deals with the techniques of hematologic study. It includes methods of collection and preparation of hematopoietic tissues; the utilization of electron, phase, polarized, fluorescent, and ultraviolet microscopy; the application of cytochemical techniques; and the methods of experimental cytology as applied to blood cells. Part 2 is devoted to general observations on the pathophysiology of hematopoietic cells. Part 3 is a detailed analysis of the different blood cell series as revealed by the present day morphologic techniques.

The book is replete with splendid photomicrographs obtained by phase contrast and electron microscopy, and the detail pictured is exciting. It demands of the reader a revitalized understanding of morphology if, in the words of the author, ". . . for no other reason than that the techniques and what they will disclose belong to the future."

The bibliography is well chosen and contains numerous review references. Nomenclature is at times awkward, but the translator is to be commended for an excellent job in a field in which nomenclature is frequently at best an awkward situation.

This book is highly recommended to the hematologist. As a source book in morphologic hematology, its scope and detail are masterful.

—*Walter A. Rambach.*

CURRENT TEACHING OF ELECTROCARDIOGRAPHY emphasizes the analytic rather than the empiric approach, the premise being that the electrocardiographer who understands "why" a given alteration occurs will be able to employ this diagnostic medium in a more definitive and accurate manner than one who has merely memorized a series of patterns each of which has been assigned to a given anatomic or physiologic abnormality. Application of this technique is predicated upon some knowledge of the basic electrophysiology of cardiac muscle, and most standard textbooks of electrocardiography present this facet of the subject in greater or lesser extent. However, to my knowledge, none probes so deeply and so critically into this particular aspect of electrocardiography as the text *New Bases of Electrocardiography*[8] by Demetrio Sodi-Pallares.

The author is the Chief of the Department of Electrocardiography at the National Institute of Cardiology in Mexico where investigators have been especially active for the past decade in exploring fundamental electrocardiographic problems. In essence, the book represents scholarly summarization of this work integrated with respect to previous concepts as well as to the findings of contemporary researchers. Although it should not be misconstrued as an all inclusive text of clinical electrocardiography (the entire field of the arrhythmia is intentionally omitted) it covers a wide area of electrocardiographic interest in an unusually definitive fashion. Mathematic and physical principles pertaining to electrocardiography are reviewed in detail. The contributions of Einthoven, Wilson, Lewis, and others are described and criticized in light of more recent investigations. The newer techniques of vectorcardiography and intracavitary electrocardiograms are presented as well as the considerable information concerning the activation process of the human heart that has been obtained by the latter technique. The data derived by these methods in various clinical entities are discussed. The ventricular gradient is defined in lucid terms and its clinical value assessed. Findings from the author's own institution of special clinical interest include Cabrera's ventricular overloading theory which demonstrates the value of the electrocardiogram in permitting hemodynamic as well as anatomic correlation; and his studies on bundle branch block by means of a bipolar intracavitary electrocardiogram with leads placed on each side of the interventricular septum.

—*Gerry A. Smyth.*

IT IS THE OCCASIONAL LOT of the reviewer to consider a book which is wholly delightful from start to finish, and so absorbing that his task is complete almost before he is aware that it has started. *Monro Kerr's Operative Obstetrics*[9] is such a book. The author of this superlative text, J. Chassar Moir, is a distinguished obstetric scholar and practitioner. His wide experience and his unusual ability as teacher and author are among the factors which make this particular volume unique among obstetric texts.

This is by no means an undergraduate text, having been prepared for "obstetricians trained and in training." It carefully avoids discussion of the anatomy, basic physiology, and all other fundamental material which is included in the usual texts that introduce the student to the field of obstetrics, and is concerned only with the most beautifully meticulous considerations of the evaluation and management of obstetric problems, abnormalities, maneuvers, and surgical procedures. The book is astonishingly complete, giving detailed consideration and critical evaluation not only of standard problems, but also of unusual attendant occurrences, and is replete with the many devices for their solution which are the mark of the obstetrician of great experience.

In addition to the actual subject matter, two other factors of great importance to this book must be mentioned. First, the author's style of writing. Monroe Kerr, in previous editions, achieved an unusually direct and intimate means of expression which takes the reader directly to the case at hand, and creates

[7] CYTOLOGY OF THE BLOOD AND BLOOD-FORMING ORGANS. By Marcel Bessis. Translated by Eric Ponder. New York and London: Grune & Stratton, 1956.

[8] NEW BASES OF ELECTROCARDIOGRAPHY. By Demetrio Sodi-Pallares, M.D. With the collaboration of Royall M. Calder, M.D., Editor, English Translation. 727 pages, 523 illustrations. $18.50. St. Louis: The C. V. Mosby Co., 1956.

[9] MONRO KERR'S OPERATIVE OBSTETRICS. Edited by J. Chassar Moir. Hon. LL.D., M.A., M.D., F.R.C.S. (Ed.), F.R.C.O.G. 6th ed. 1,008 pages, illustrated $20.00. Baltimore: Williams & Wilkins Co., 1956.

the air of personal discussion in which the reader seems to participate. Chassar Moir has also this remarkable ability, which is handsomely illustrated in the several sections which have been either entirely rewritten, or significantly amended. Secondly, the text is beautifully supported throughout by succinct case reports to illustrate the matters under consideration, and by pertinent recent and historical reports from the literature which are critically evaluated.

In a book of uniform excellence it is not possible to select any one section which is outstanding; all are outstanding. This book should be read in its entirety by all obstetric residents. Obstetricians will find it an absorbing and highly rewarding experience to browse among its pages, or, as I have done with the greatest satisfaction, to read from cover to cover.

The illustrations, mostly pen and ink, are very informative and well selected, the format is attractive, and the type highly legible. The paper and binding are of excellent quality. —*David N. Danforth.*

THE VERY READABLE MONOGRAPH *Anesthesia for Surgery of the Heart*[10] is more than a guide to anesthetic management of heart surgery. It presents a philosophy of patient, surgeon, anesthesiologist, internist, relationship which could be adopted in other fields of surgery with great benefit to all concerned, especially to the patient. It points out the duties and obligations of the anesthesiologist who is a conscientious, well rounded consultant, and not just an operating room technician.

The physician interested in heart surgery will find the chapters of "History" and "Selection Of Patients" both interesting and instructive. The chapters on "Preliminary Medication" and "Anesthesia Management" stress fundamental principles that are applicable to any good anesthetic procedure. The author's preferred technique is covered in considerable detail in the chapter on "Management," and the entire chapter is an excellent reference for both the novice and the experienced cardiac anesthesiologist.

The short (6 page) chapter on "Cardiac Irregularities" merits the special attention of both surgeons and anesthesiologists. It contains a wealth of useful information on one of the most frequent and disconcerting complications occurring in the operating room. Other anesthetic complications and postanesthetic care are discussed briefly but adequately.

Emphasizing the need for a thorough understanding of cardiac anomalies by the anesthesiologist, the author devotes a short chapter to each of the congenital and acquired heart lesions which are most frequently encountered.

The entire book is written in clear, concise language which is easily understood and followed. It should be in the library of every anesthesiologist and cardiac surgeon. —*William O. McQuiston.*

THE VOLUME entitled *Chirurgische Indikationen*,[11] edited by Walter Hess and published by Georg Thieme, Stuttgart, Germany, is dedicated to Professor Rudolf Nissen by many of his present and past associates in honor of his sixtieth birthday. It is a tribute to Nissen's outstanding work in Munich, Berlin, Istanbul, New York, and Basel, and a thoughtful reminder of the volume published in 1937 under the same title.

Fifty-four European and American authors, many of them members of the International College of Surgeons, have contributed to the 45 papers constituting this attractive volume. In most instances, the publications appear in the author's own language which may actually present a challenge to the reader who cannot easily fight his way through English, French, German, Spanish, and Italian.

It is impossible for a reviewer to give in a limited space an extensive and complete account of all the excellent articles presented by authors who have long been known as experts in the fields they discuss. The material, condensed in 9 chapters, deals essentially with recent improvements in surgery and surgical specialties, all of which have largely developed since Nissen's original publication 20 years ago. The title of this book might therefore be misleading, for its contents concern rather selected topics. A first chapter on generalities emphasizes surgeon-internist teamwork, operability, the notion of immediate and delayed emergencies, social indications, antibiotics, and the use of newer methods of anesthesia. Under surgery of the heart, the physiologic basis of heart surgery, surgery of the mitral valve, and pericardiectomy are discussed. A discussion of surgery of the lungs and esophagus is essentially concerned with the treatment of carcinoma and bronchiectasis. Carcinoma of the stomach and the problems of management encountered in massive gastric bleeding and the postgastrectomy syndrome are dealt with under the heading gastric surgery. The chapter on surgery of the biliary tree, spleen, and portal vein includes a discussion of the indications for sphincterotomy, reintervention on the biliary tree, splenectomy, acute cholecystitis, and portal hypertention. In the section on urology much interest is shown in the use of nephrectomy in cases of hypertension, the surgical management of the atonic bladder, indications for the various methods of prostatectomy, and transplantation of the ureters. Carcinoma of the breast and cancer of the female genitalia both are considered under the heading gynecologic surgery. The chapter on surgery of the extremities is limited to considerations of such problems as indications for plastic replacement of the femoral head, bone tumors, peripheral nerve surgery, and sympathectomy in peripheral vascular disease. Finally, under neurosurgery, endocrinology, and ophthalmology interesting papers can be found regarding surgical indications in cases of pseudotumor cerebri, severe cerebral injuries and pituitary adenomas, surgical treatment of detachment of the retina, and a discussion on the influence of prophylactic iodine therapy on the indications for surgical treatment of nontoxic nodular goiters in an endemic area.

In brief, *Chirurgische Indikationen* is not a textbook as its title may lead one to believe. This well edited, well illustrated, and attractively presented volume will serve as an excellent reference to a well supplied medical library. —*Fernand R. Schmidt.*

[10] ANESTHESIA FOR SURGERY OF THE HEART. By Kenneth K. Keown, M.D., F.A.C.S. 109 pages, illustrated. Springfield: Charles C Thomas, 1956.

[11] CHIRURGISCHE INDIKATIONEN. By Rudolf Nissen. Edited by Walter Hess. 299 pages, 15 illustrations, and 9 tables. DM42.—Stuttgart: Georg Thieme Verlag, 1956.

IN AN IMPRESSIVE COMPREHENSIVE VOLUME, *Vigesimoseptimo Congreso Argentino de Cirurgia*,[12] the proceedings of the 27th Congress of the Argentine Surgical Society are recorded. The week-long meeting consisted of presentation of papers, discussions, and panel reviews.

Among the subjects presented in the first plenary session was tumors of the parotid, a masterly work by Dr. K. Herrero. DuCloux' congenital equinus varus was discussed during the second plenary session, whereas surgical treatment of pulmonary tuberculosis was the theme of the third meeting.

These papers comprise the entire volume of 409 pages, and are remarkable because of their detailed coverage of the subjects. Assuredly, an advanced surgery is practiced in Argentina as evidenced by these contributions.

In the resection of the parotid, the technique of R. Finochietto or A. Gutierrez is followed. In the case of benign tumors, definitive surgical treatment gave invariably good results, whereas malignant and mixed tumors did not fare as well.

Regarding equinus varus, the angulation was studied by employing mathematic principles and calculations, and only after the degree of correction was ascertained was surgical correction through osteotomy attempted. The technique was always performed according to one of the more accepted orthopedic procedures.

Tabulation of the results of pulmonary resection for tuberculosis in 287 cases showed a cure rate of 86.5 per cent, 55 of the patients being treated by pneumonectomy, 175 by lobectomy, and 57 by segmental resection. —*Stephen A. Zieman.*

[12] VIGESIMOSEPTIMO CONGRESO ARGENTINO DE CIRUGIA. Fasciculo I: Relatos Oficales. President, Dr. Jose A. Caeiro. 409 pages, illustrated. Published under the direction of Dr. Alfredo Llambias. Buenos Aires: En La Secretaira de la Asociacion, 1956.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

THE HUMAN BRAIN; FROM PRIMITIVE TO MODERN. By A. M. Lassek, M.D., Ph.D. 242 pages. $4.75. Springfield, Ill.: Charles C Thomas, 1957.

MOVEMENT OF THE HEART AND BLOOD IN ANIMALS. An Anatomical Essay by William Harvey. Translated from the original Latin by Kenneth J. Franklin and now published for the Royal College of Physicians of London. 209 pages, illustrated. $3.50. Springfield, Ill.: Charles C Thomas, 1957.

THE YEAR BOOK OF CANCER (1956-1957 YEAR BOOK SERIES). Compiled and edited by Randolph Lee Clark, Jr., M.D., M.Sc.(Surg.), D.Sc.(Hon.), and Russell W. Cumley, Ph.D. 572 pages, illustrated. Chicago: Year Book Publishers, Inc., 1957.

FUNDAMENTALS OF HUMAN PHYSIOLOGY FOR STUDENTS IN THE MEDICAL SCIENCES. By W. B. Youmans, Ph.D., M.D. 567 pages, illustrated. $8.50. Chicago: Year Book Publishers, Inc., 1957.

MEDICAL RADIATION BIOLOGY. By Friedrich Ellinger, M.D. 945 pages, illustrated. $20.00. Springfield, Ill.: Charles C Thomas, 1957.

FROM STERILITY TO FERTILITY; A GUIDE TO THE CAUSES AND CURE OF CHILDLESSNESS. By Elliot E. Philipp, M. B., B.Chir., F.R.C.S., M.R.C.O.G. 120 pages, illustrated. $4.75. New York: Philosophical Library, 1957.

MODERN PERINATAL CARE. By Leslie V. Dill, M.D., F.A.C.S. 309 pages. New York: Appleton-Century-Crofts, Inc., 1957.

DIE VASKULAEREN ERKRANKUNGEN IM GEBIET DER ARTERIA VERTEBRALIS UND ARTERIA BASIALIS; EINE ANATOMISCHE UND PATHOLOGISCHE, KLINISCHE UND NEURORADIOLOGISCHE STUDIE. By von H. Krayenbühl and M. G. Yasargil. 170 pages, 127 illustrations. Stuttgart: Georg Thieme, 1957.

ANESTHESIA; A MANUAL FOR STUDENTS AND PHYSICIANS. By Stuart C. Cullen, M.D. 5th ed. 295 pages, illustrated. $5.50. Chicago: Year Book Publishers, Inc., 1957.

METHODS IN SURGICAL PATHOLOGY. By Henry A. Teloh, M.D. 127 pages. Springfield, Ill: Charles C Thomas, 1957.

LUCRARILE CONGRESULUI NATIONAL DE STIINTE MEDICALE MAY 1957. I. Rapoarte. Academia Republicii Populare Romine. 1363 pages, not illustrated. Bucharest: Academia Republicii Populare Romine, 1957.

NOMINA ANATOMICA. By Prof. Dr. Fr. Kopsch. 5th ed. Vergleichende Uebersicht der Basler, Jenaer und Pariser Nomenklatur. 155 pages, not illustrated. Stuttgart: Georg Thieme, 1957.

OBSTETRIC MECHANISMS AND THEIR MANAGEMENT. By John C. Ullery, M.D., F.A.C.S., and Mario A. Castallo, M.D., F.A.C.S., Sc.D.(Hon.). 306 pages, 185 illustrations. $5.50. Philadelphia: F. A. Davis Co., 1957.

SURGICAL TECHNIQUE AND PRINCIPLES OF OPERATIVE SURGERY. By A. V. Partipilo, M.D., F.A.C.S. Foreword by Alton Oschsner, M.D., F.A.C.S. 6th rev. ed. 966 pages, 719 figures containing 1,235 illustrations with 4 in color. $20.00. Philadelphia: Lea & Febiger, 1957.

FADS AND FALLACIES IN THE NAME OF SCIENCE (FORMERLY PUBLISHED UNDER THE TITLE: IN THE NAME OF SCIENCE). By Martin Gardner. 363 pages, not illustrated. $1.50. New York: Dover Publications, Inc., 1957.

THE BASES OF TREATMENT. By Neuton S. Stern, M.D., and Thomas N. Stern, M.D. 176 pages, not illustrated. $4.75. Springfield, Ill.: Charles C Thomas, 1957.

OLD DOC. By O. H. Perry Pepper, M.D. 247 pages, not illustrated. $3.75. Philadelphia and New York: J. B. Lippincott Co., 1957.

PLASTER OF PARIS TECHNIQUE. By Marian English, S.R. N., R.F.N. Foreword by D. Ll. Griffiths, M.B.E., F.R.C.S. 126 pages, illustrated. $4.00. Edinburgh and London: E. & S. Livingstone Ltd., 1957.